

# JOURNAL OF CLINICAL AND EXPERIMENTAL PSYCHOPATHOLOGY

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## *The van Ophuijsen Memorial Volume*

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## Johan H. W. van Ophuijsen

JOHAN H. W. VAN OPHUIJSEN was born on November 12, 1882, at Padang Sidempooan, Sumatra. He graduated from the University of Leiden, the Netherlands, in 1909. One of the founders of the Netherlands Psychoanalytic Society in 1917 (President, 1927-1934), he organized the first International Psychoanalytic Congress after World War I (1920) and was a member and officer of the International Psychoanalytic Association, 1925-1936. In 1935 he accepted an invitation of the Psychoanalytic Institute to come to the United States, and upon being licensed as a physician in the State of New York (1936) and named a diplomate in psychiatry by the American Board of Psychiatry and Neurology (1937), he taught at the Institute, 1938-1948. One of his first American appointments (1935) was to the psychiatric staff of the Jewish Board of Guardians, whose efforts on behalf of troubled children he guided for more than fifteen years. He was a member of the psychiatric staff of Mount Sinai Hospital (1940-1942) and Lenox Hill Hospital (1942-1946), Attending Physician in Psychiatry for the Veterans Administration (1946-1950), and Lecturer in Psychoanalytic Medicine at the Long Island College of Medicine (1949-1950). In 1950 he was named Director of the Creedmoor Institute for Psychobiologic Studies, Creedmoor State Hospital, New York, and editor of the *JOURNAL OF CLINICAL AND EXPERIMENTAL PSYCHOPATHOLOGY*. He was himself the author or co-author of some forty publications. Dr. van Ophuijsen died on May 31, 1950, at the Van Ophuijsen Center, 15 East 62nd Street, New York, of which he was a founder.

"Destiny has been good to me," Dr. van Ophuijsen said in his dedication address at the Creedmoor Institute in February, 1950. "What others may consider merit, to me appears almost as a gift. This is especially true with regard to my interest in psychiatry. Destiny arranged that I should receive my medical education at Leiden University, where the equality of psychiatry with other clinical disciplines was a long-established tradition. It gave me as a teacher none other than Jellgersma, who never failed to keep a proper balance between the purely clinical approach of Kraepelin and the penetrating psychologic dissection of Freud. That I recognized Freud's greatness a few years earlier than my teacher was again not merit but the result of what differentiates youthful enthusiasm from mature caution. When I lived at Zurich, Bleuler and his school slowly and hesitatingly let go of the so-called association psychology and adopted some of Freud's theories. A strong attachment to C. G. Jung during that period kept me from fully recognizing the value of psychoanalysis. A passing glimpse into Pavlov's laboratories kept awake my interest in the physiology of psychiatry. From 1915, the year in which I emancipated myself from Jung's influence, to the present time, I have had no reason not to consider Freud my teacher—that same Freud who as early as 1914 had said: 'We must bear in mind that some day all our provisional formulations in psychology will have to be based on an organic foundation. It will then probably be seen that it is special chemical substances and processes that achieve the effects of sexuality and the perpetuation of individual life in the life of the species.'

"It was again destiny's gift that permitted me to enter this country. A deep gratitude has since then pervaded me and prompted me to pay my debt by giving as much as possible of what I have to give. What I consider an additional reward came three years ago. . . . At an age when most men think of retiring I was asked to start something new and fascinating—the biochemical research which my teacher Freud would have chosen for his next incarnation!"

## ETERNAL NOW

They shall not say that you have died  
Or that you stayed behind,  
For quietly you turned aside  
And tread upon eternity.

Nor can the cold unfriendly tang  
Of freshly spaded earth  
Chill the golden notes you sang  
Or the heart which now is still.

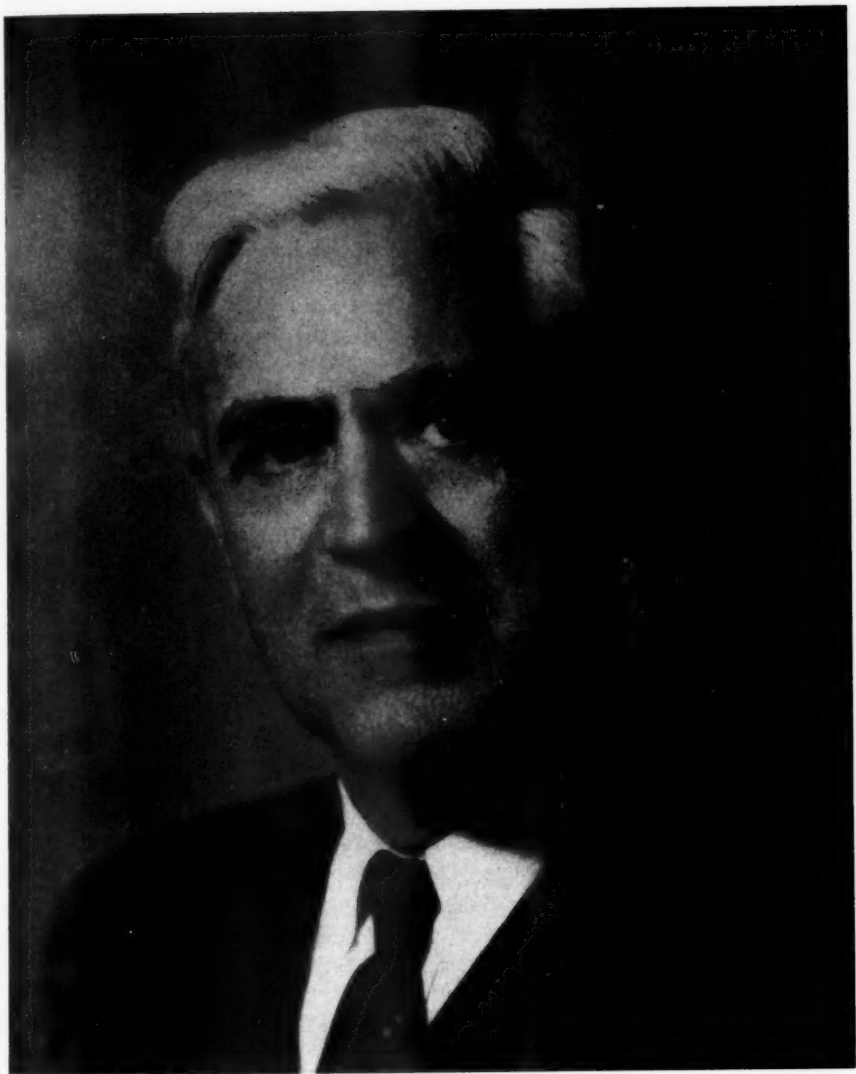
So turn your back upon the grave  
And sing your sky-bound song,  
Lest dank earth mute the heart which gave  
Sunlight to the day.

And send your laughter through the rain  
Of tears which ever flow,  
For many years shall wax and wane  
Before I let you go.

J. G.

*June, 1950*





Johan H. W. van Ophuijsen  
1882 - 1950

## Eulogy Delivered at the Funeral of Johan H. W. van Ophuijsen on June 3, 1950

OUR hearts are too heavy for our voices, our grief is inconsolable. Beloved teacher and colleague, friend and father, we cannot speak of leavetaking for you have taken so much of us with you and left so much of you with us. Your pioneer and scholarly father and your warm and devoted mother labored well—they gave to all races and to all creeds a staunch champion. A good man who really knew the basic right from wrong, you simply did the right. A brave man who deeply appreciated the fundamental dignity and rights of man, you were always unhesitatingly ready to fight for them. In these critical times, the world sorely needs men like you—our loss is grievous.

You gave unstintingly of yourself to those who needed you. Your compassion went out to all who wanted help; even so, you kept a special niche in your heart for children, for they are the most helpless. Your feelings were so sensitive that you could sense all the important little things even as your broad vision could comprehend the most majestic.

You understood the essence of a hurt; where it hurt and how it hurt and why it hurt. You understood the ultimate meanings—the meanings of devotion and dedication, of independence and integrity, of sympathy and support. You were so rich in gentleness and patience. Your students knew it, every patient sensed it. You could ease suffering so well having yourself suffered so much. You were a great scholar of the spirit and healer of the mind.

You were a brilliant clinician following in the tradition of your honored Jelgersma. Psychopathology stood out for you with such vivid clarity. Pioneer psychoanalyst, you were ever faithful to your beloved teacher and friend, Freud. You had the true courage of conviction—the courage to tenaciously defend and advance the principles you knew to be true—and the courage to face and to study, to accept and propound new facts, new ideas and new conceptions. In these, you saw the stirrings of continuing fresh life for that which to you was life itself, your very breath, your every act—the humanity and science of psychiatry.

You were so great a teacher that, though the time was short, your work will go on. Since so much of your life was in your work, through it you will continue to live. You had the precious gift to instill life even into the inanimate—your Center and your Institute and your Jewish Board of Guardians are the living embodiment of your dreams and your ideals. You were ever reverent but ever the rebel. Your wisdom was the ageless wisdom of our elders even as your boldness and vigor and freshness in thinking were the priceless heritage of everlasting youth. You were at the peak of your wisdom, steeped in the midst of full creative activity and giving of your great contributions, when our bereavement came. To the very last moment you worked and planned with the unquenchable enthusiasm that springs from youth.

You were a man—a man who appreciated the beauty that is in man and by man. How you partook in the many lands and cultures you came to know and admire. How you thrilled to the music that you knew so well and played so well. How you treasured poetry and how beautifully you could write it. How proud you were of your participation in the Olympic Games. How you gloried in the sound of water lapping the hull of a boat and the wind against its sails. How you loved the spring and its flowers with their promise of perpetual youth. Your humility was matched only by your graces—and they were so many. It was our tragedy that your humanity was too great for one human heart. Few men were as deeply loved by those about them and no man more richly deserved this love. To you are dedicated the finest shrines that man can dedicate to man—the hearts of those who loved you and the very beings of those who were privileged to work with you.

You have justly earned your rest and your peace.

# JOURNAL OF CLINICAL AND EXPERIMENTAL PSYCHOPATHOLOGY

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## A New Phase in Clinical Psychiatry

### PART I AND INTRODUCTION

#### ENDOCRINOLOGIC ORIENTATION TO PSYCHIATRIC DISORDERS

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Having been requested to open the discussion with a few introductory remarks, I would like to outline briefly a frame of reference. With your permission, I will, in doing so, make use of some personal reminiscences, chosen from various phases of my psychiatric experience.

In the summer of 1927, I visited Freud at the Semmering near Vienna, where he was spending most of his vacation. Steinach was there, too, at that time and I remember very vividly Freud stating in reaction to some opinion I had expressed: "Of course, you know, I am firmly convinced that one day all these disturbances we are trying to understand will be treated by means of hormones or similar substances. I am glad it is not yet that far, as it gives us the opportunity of investigating what might otherwise be overlooked." This statement startled and disappointed me. It sounded to me almost as though he had become untrue to himself. I had not yet learned to appreciate fully the greatness of this man who had staked out his chosen task and consistently worked at it without losing sight of its significance in relationship to the entire field of psychiatry. Certain other of his utterances might have reminded me during the previous fifteen years of Freud's self-limitation, but I did not heed them.

It should, therefore, not surprise you that exactly twenty years ago, on the occasion of the first International Congress of Mental Hygiene at Washington, D. C., I was very much offended

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by what I considered a derogatory remark Adolf Meyer made on psychoanalysts. Regardless of whether the remark as such was correct or not and, if correct, justified or not—regardless, also, of the question whether Adolf Meyer understood and evaluated psychoanalysis properly or not—my emotional reaction indicated that I did not appreciate his unique significance in the development of American psychiatry.

Again, I could say I should have appreciated his significance, for my psychiatric education by Jellgersma was based on Emil Kraepelin's approach. Overholser states about Kraepelin, "His great contribution was that at last he had brought psychiatry into medicine." And Zilboorg says, "He established the fact that mental disease, like any other disease . . . is a disease running a regular course." In other words, Kraepelin introduced and consistently followed the true clinical approach. I had been taught this for years. For even after Jellgersma had accepted Freud's findings he was never tempted into leaving the straight and narrow path of careful clinical observation. Other followers of Freud, however, were tempted, and soon understandable psychologic connection, unconscious of course, became equivalent with psychogenic causality. This did no harm as long as psychoneuroses were concerned—it was harmful, however, as soon as the analyst's interest turned to certain psychoses and even to such non-psychotic disturbances as sexual and other conduct disorders, acquired or inherent. It led to the neglect of a large amount of clinical knowledge which would have warned against hasty conclusions of the nature I characterized before.

It was only after having been in this country for some time that I recognized the danger Adolf Meyer had been fighting. I don't feel competent to decide whether it was wise or not to introduce a new terminology in order to teach clinical approach, the scope of which, of course, had widened very considerably since Kraepelin's days. Nor do I feel competent to decide to what extent Adolf Meyer's efforts have been successful. However, one thing is certain: it took the experiences of another world war to bring about the general acceptance of psychiatry with an equal status to that of the other clinical disciplines in the curriculum of our medical schools. Be that as it may, I learned to consider Adolf Meyer as the outstanding psychiatrist who held on to the solid foundation of clinical facts when others appeared to be more interested in psychologic processes only. It is for this reason that the institute in which the research is carried out, about which others will report, is called an institute for psychobiologic studies.

There are indications that the pendulum of interest which swung so far in the direction of the so-called dynamics of a psychologic nature will soon swing back in the direction of physical phenomena and probably of biochemical disturbances in particular. It would lead us too far afield to discuss what these indications are and why such a change of direction should take place at this time. It is certain that, after the behavior disorders and psychoneuroses, the schizophrenias are receiving more and more attention—and rightly so, as they still claim an enormous number of victims.

Speaking of the schizophrenias gives me an opportunity to illustrate a point I was making before. Those of you who are acquainted with the so-called official classification of psychiatric disorders know that the schizophrenias are grouped together with the psychoneuroses. This is evidently the result *not* of clinical thinking, but of thinking in terms of neuropathology: "No structural change can be found in either; for the time being they belong in the same group." The

clinician would say: "These two forms of pathology are as different as day and night. The etiology of psychoneurosis is always psychic, its course is determined by psychic influences and it never ends in deterioration. The etiology of schizophrenia is as yet unknown, its various forms in terms of chronologic development and symptom picture suggest very strongly the probability of an auto-intoxication, possibly of endocrine origin, and in by far the greater majority of the cases deterioration is the final outcome." This is something the clinician has been saying for about fifty years. My teacher, Jellgersma, used to put his recognition of the psychodynamics and the physical etiology together in the ugly, but not unpicturesque statement: "Schizophrenia is hysteria plus intoxication."

As in the case of the schizophrenias, the clinician would never think of grouping the manic-depressive psychosis with the psychoneurosis merely on the ground of absence of demonstrable structural change. In a sense, the manic-depressive psychosis is the contrast of the schizophrenia, because regardless of the seriousness and duration of the episodes it never leads to deterioration; the prognosis of each single episode is good. For this reason my collaborators have chosen schizophrenia and manic-depressive psychoses as the principal material for their investigations. They added the involuntal psychosis. The reason for this choice should be evident: its etiology is undoubtedly some endocrine disturbance which leads to a symptom picture with many features in common with that of schizophrenia, but in uncomplicated cases it has a favorable prognosis.

Research in this field should accept the guidance and conditions imposed by the knowledge of clinical facts, if it does not want to go astray as did psychoanalysis whenever it refused to accept this control. Our knowledge of the clinical facts is certainly not complete, but enough is known to write a roughly accurate outline of the pathobiography of the three psychoses mentioned before. This outline has to serve as a constant means of orientation to the researcher. As soon as he has the tendency to question the clinical facts and deductions on the basis of his findings only, he can be certain that he is wrong. Clinical experience of the proper kind can only be modified by more clinical experience of the proper kind. It requires that research in this field take into account the processes of growth, maturation and involution, interpreting findings in terms of phases of development.

I hope that the following discussions will show how research can be directed by clinical knowledge without overlooking problems it has the task to solve.

#### RESUMEN

El Dr. van Ophuijsen recuerda que durante el verano de 1927 Freud le "desconcertó" con la siguiente declaración: "Desde luego, usted sabe que yo estoy firmemente convencido de que algún día todos estos trastornos que estamos ahora tratando de comprender, serán tratados con hormonas o con otras sustancias similares. Celebro que aún no hallamos llegado tan lejos; ya que ello nos ofrece la oportunidad de investigar lo que, de otra forma, se hubiera pasado por alto."

El autor rinde homenaje a Kraepelin, que "introdujo y empleó de un modo constante los auténticos métodos clínicos." También rinde tributo a Adolf Meyer, que "se mantuvo sobre los sólidos cimientos de los hechos clínicos, cuando otros investigadores parecían estar más interesados en los procesos psicológicos." Observa el autor que el péndulo de interés que osciló hasta el

extremo en la dirección de la psicodinámica, oscilará nuevamente hacia su punto de origen en la dirección de los fenómenos físicos y, probablemente, de los trastornos bioquímicos en particular.

El Dr. van Ophuijsen aconsejó que se investigara en el campo de la Psiquiatría, para "aceptar la guía y las condiciones impuestas por el conocimiento de los hechos clínicos, si no se desea extraviarse como sucedió al Psicoanálisis cuando se negó a aceptar esta orientación".

## RESUME

Le Dr. van Ophuijsen rappelle que, au cours de l'été de 1927, Freud l'avait extrêmement surpris en lui déclarant: "Evidemment, je suis fermement convaincu qu'un certain jour, tous ces troubles que nous essayons de comprendre seront traités au moyen d'hormones ou de substances analogues. Je suis heureux que nous ne soyons pas aussi avancés car nous avons ainsi la possibilité d'étudier ce qui, autrement, pourrait être négligé."

L'auteur rend hommage à Kraepelin, qui "a introduit et suivi constamment la méthode clinique véritable" et à Adolf Meyer qui "s'est appuyé sur la fondation solide du fait clinique, tandis que d'autres semblent avoir été plus intéressés par le processus psychologique seul". Il signale que le pendule de l'intérêt, qui a si fortement oscillé dans la direction de la soi-disant dynamique de nature psychologique, reviendra bientôt en arrière dans la direction des phénomènes physiques, des altérations biochimiques en particulier.

Le Dr. van Ophuijsen recommande que la recherche, dans le domaine de la psychiatrie: "accepte la direction et les conditions imposées par la connaissance des faits cliniques si elle ne veut pas être entraînée dans une fausse direction comme cela s'est produit pour la psychanalyse chaque fois qu'elle a refusé de se soumettre à ce contrôle."

# An Appraisal of the Current Status of Histamine Biochemotherapy in Psychiatry and the Theoretical Significance of its Effects

## PART II

### ENDOCRINOLOGIC ORIENTATION TO PSYCHIATRIC DISORDERS

*Raymond R. Sackler, M.D., Mortimer D. Sackler, M.D.,*

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The biochemotherapeutic approaches to psychiatric disorders demand critical consideration for three reasons:

1. The therapeutic successes thus far achieved represent real opportunities for arrest of malignant processes in an appreciable percentage of patients.
2. The biologic data which they make available indicate that certain psychotic processes, the so-called functional psychoses and involutional psychoses, are associated with a number of physiologic phenomena some of which:
  - a. show distinct differences in the psychotics, as a group, and the psychoneurotics, as a group;
  - b. vary with the severity of the psychotic process, and
  - c. are altered by the biochemotherapies and suggest interesting correlations between the character of the changes and attainment of improvement.
3. The findings also suggest neuroendocrine dysequilibria, the study of which may unravel some of the chemical processes whose effects upon neuronal metabolism possibly result in psychotic manifestations.

### WHAT IS HISTAMINE?

Since its isolation from soy bean in 1909 by Yoshimura,<sup>1</sup> and its identification in ergot by Barger and Dale<sup>2</sup> in 1910, histamine (B-iminozylethylamine) has been intriguing physiologically and enigmatic therapeutically. Despite the fact that many thousands of experiments have probed and almost as many reports have discussed its physiology and pharmacology just as recently as 1945, authorities<sup>3</sup> described this decarboxylation product of the amino acid histidine as "of considerable academic interest but little therapeutic importance." Research of the past few years — particularly in the field of psychiatric and neuroendocrinologic disorders — may soon enable us to accord this substance its place as a vital agent playing a major physiologic role both in body economy and in the treatment of metabolic disorders.

Presented at a Round Table Dinner Meeting, 106th Annual Meeting of The American Psychiatric Association, Detroit, Michigan, May 1, 1950

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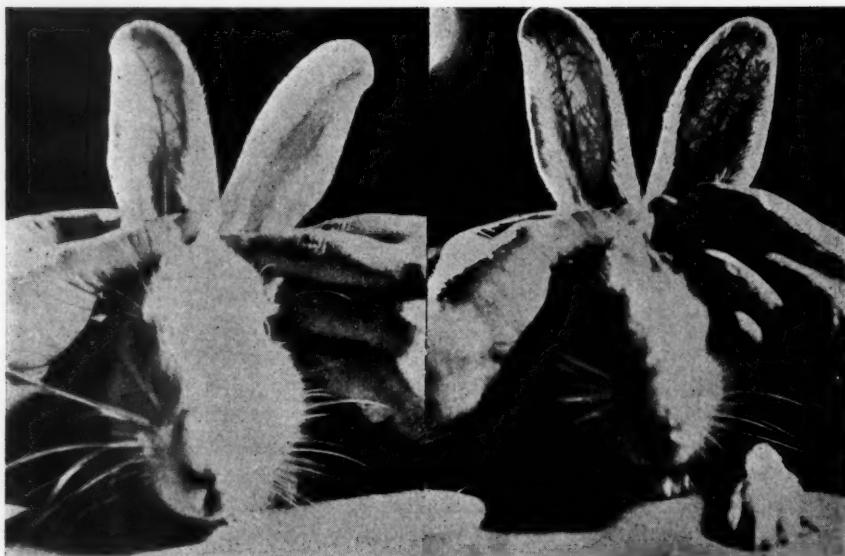


FIG. 1. *Left*: Photograph immediately after shocking current was applied to the right ear. Note vasodilatation of the right ear and no change in left ear. *Right*: Short time later, note vasodilatation of both ears.

#### HOW HISTAMINE CAME TO BE USED IN PSYCHIATRIC THERAPY

Our biochemotherapeutic application of histamine to psychiatric disorders was neither fortuitous nor empirical. During an attempt to elucidate the beneficial mechanisms of ECT, the passage of "shocking current" through living tissue suggested the liberation of a blood-borne vasodilating agent (Fig. 1). This led to a series of experiments and observations, some of which have been previously recorded:

1. A high incidence of achlorhydria and hypochlorhydria in psychotic patients.<sup>4</sup>
2. The elevation of gastric acidity produced by ECT (Electro-convulsive therapy).<sup>5, 6</sup>
3. The administration of histamine,<sup>7-10</sup> to a series of schizophrenic, manic-depressive and involutional psychotics and the finding that:
  - a. histamine alone gave clinical results comparable to those attained with ECT controls, and
  - b. doubled the convalescent status rates when it was followed by ECT in histamine-refractory patients.

Thus, the series of events which led our group to the therapeutic application of histamine differed in several ways from that which attracted other workers to its use.

The pioneering work of Marshall and Tarwater<sup>11</sup> in 1938 was based on a theory of "psychoallergy"; they believed that histamine could act as a non-specific desensitizing agent. In addition,



they felt that it could also be beneficial as a mild form of shock treatment. The following year, Marshall again reported<sup>12</sup> on histamine in the treatment of psychiatric disorders.

Horace Hill,<sup>13-15</sup> Britain's staunch advocate of histamine, based his original work on a clinical interpretation of ECT. He noted that some symptoms of shock could be produced by histamine, others by insulin. In addition, he aimed to achieve cerebral vasodilation and increased permeability to allow for the passage of necessary nutrients. Robb and his co-workers<sup>16</sup> utilized histamine with the specific aim of inducing vascular shock.

#### WHAT CLINICAL ACHIEVEMENTS HAS HISTAMINE RECORDED IN PSYCHIATRY?

In the more than 500 psychiatric patients who have received some form of histamine biochemotherapy, improvement has been recorded in from 24 per cent to over 50 per cent depending on the series studied. This compilation includes the several series<sup>7, 8, 11-19</sup> reported in the literature by the authors and by others, a large number (over 200) unreported non-hospitalized psychiatric patients of the authors and unreported hospitalized psychotics treated by Horace Hill.<sup>20</sup> The reports are, for these states, remarkable in their practical unanimity as to its value, despite the fact that the "improvement rates" recorded ranged from 24 per cent (in our series of hospitalized psychotics) to over 50 per cent. When used in conjunction with other therapies, a more uniform 50 per cent to 60 per cent improvement rate is noted. Statistical reconciliation and appraisal of the over-all results from diverse sources is difficult because of differences in severity and duration of the disease processes and the practical impossibility of assessing the different criteria used for denoting "improvement." The only negative reports relating to the psychiatric application of histamine are: one on cerebral arteriosclerotics,<sup>18</sup> and a report on three catatonic schizophrenics.<sup>17</sup>

Appraisal of the data at hand suggests:

1. That histamine alone affords a non-convulsive biochemotherapy for selected psychiatric disorders as effective as ECT.
2. That histamine-refractoriness does not indicate refractoriness to other therapeutic procedures, on the contrary, histamine pre-treatment enhances the effectiveness of certain other procedures, i.e., ECT and sub-coma insulin.
3. That the use of therapies in series, i.e., histamine, followed by ECT or by insulin doubles the number of patients improving and attaining convalescent status in some series.
4. That the earlier the treatment, the greater the chances for success.
5. That histamine biochemotherapy is free from the undesired side-effects of ECT and insulin coma, is easy to administer and requires less special apparatus.

#### WHAT IS THE CHARACTER OF THE CLINICAL IMPROVEMENT WITH HISTAMINE BIOCHEMOTHERAPY?

Improvement, when achieved, varies qualitatively and quantitatively. In a few patients the response may be dramatic, but in most cases the changes are subtle though definite. Some patients show alleviation of one group of symptoms, while in others, these same symptoms persist. A number of generalizations may be made as to the character of the responses when they occur.

Subjective changes reported by patients are greater alertness, the ability to think more clearly and to function more efficiently. Irritability, anxiety and depression are reduced to a fairly marked degree. Auditory hallucinations have been observed to disappear often within a matter of days, in some cases, even following failure of ECT to affect the perceptive disorder. Appetite is usually improved and insomnia diminished.

The objective changes as noted by relatives include improvement in behavior, personality and sociability. These often antecede subjective recognition of change by the patient. Schizophrenic patients who respond to treatment show a lessening or total absence of bizarre activity. Whereas, previous to therapy, hospitalization may have been seriously considered by the family as inevitable, following one to two weeks of treatment, this recourse is often rejected as unnecessary. The improved patients become more conscious of appearance and personal hygiene, show more interest in their surroundings, work and hobby, and express more warmth toward parents and family. They participate more willingly in day-to-day activities.

(The improvement as noted on psychological testing — Rorschach, Figure Drawings, Thematic Apperception Test and Bellevue Wechsler — is reported in Part IV.)

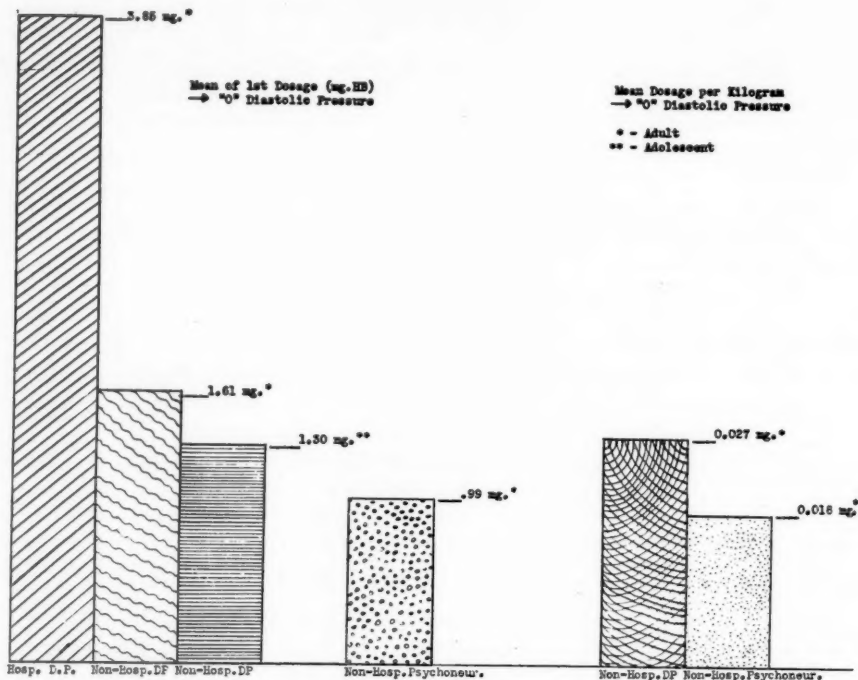


FIG. 2. Histamine tolerance—hospitalized and non-hospitalized schizophrenics and psychoneurotics.

### WHAT SIGNIFICANT BIOLOGIC DATA HAS HISTAMINE BIOCHEMOTHERAPY REVEALED?

While detailed analysis of all the data of our different histamine studies has yet to be completed, preliminary conclusions are herewith presented for purposes of discussion:

1. Differences in histamine tolerance seem to demarcate biochemically the psychotic from the psychoneurotic categories, e.g., as a group, schizophrenics appear to tolerate at least 50 per cent more histamine than the psychoneurotics. (Fig. 2)

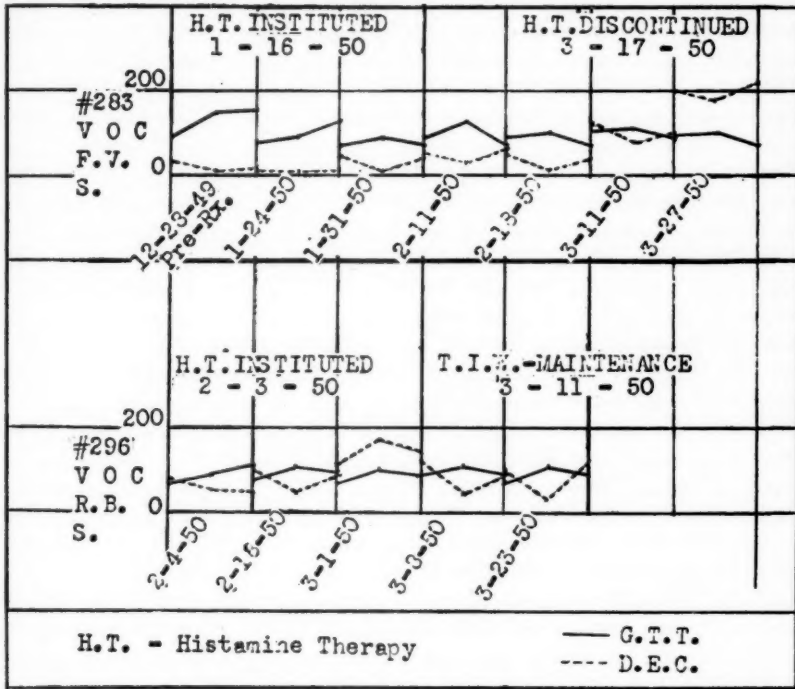


FIG. 3. Effect of histamine on glucose tolerance (Exton-Rose procedure) and eosinophile response to administered glucose. (DEC = direct eosinophile count.)

2. Histamine tolerance varies with severity, e.g., hospitalized vs. non-hospitalized psychotics.
3. Histamine tolerance seems to be increased in the presence of agitation.
4. Histamine tolerance seems to be reduced by:
  - a. The sex steroids
  - b. Thyroid
5. Histamine apparently influences other physiologic functions: (Fig. 3)
  - a. Glucose tolerance
  - b. Eosinophile response to orally administered glucose.

There has been no evidence of any change in EEG records of eight hospitalized patients given a course of histamine therapy. These data are being reported elsewhere.

#### SOME PHYSIOPATHOLOGIC PATTERNS SUGGESTED BY THE FINDINGS IN HISTAMINE BIOCHEMOTHERAPY

In our search for a common mechanism for the therapeutic effectiveness of histamine and of other modalities, our observations indicated that a histamine deficiency—either absolute in a quantitative sense or relative functionally—might be a causative factor in psychotic processes. They further suggested that both insulin therapy and ECT acted in whole or in part through histamine liberation. Interestingly, Billig and Hesser<sup>21</sup> had already reported that insulin coma therapy causes a rise in blood histamine levels and that the coma is related more to this level than to the blood sugar fall.

Early in our studies, we attempted to explain the beneficial effects of our direct histamine therapy by a hypothesis which was formulated on the basis of the facts and concepts then at hand. It was stated somewhat as follows: Psychotic manifestations were the end result of neuronal metabolic disturbances arising from a chain of adverse events in part attributable to cerebral vasoconstriction or impaired capillary permeability, leading to improper oxygenation and ultimately to metabolic anoxia. The vasodilating effects of histamine on the cerebral vessels were thought to contribute at least in part to the correction of these disturbances.

Not being completely satisfied that this concept contained the entire answer, we re-examined it as the following additional data became available:

The significance of achlorhydria and hypochlorhydria was underlined as a statistical study<sup>22</sup> and revealed an almost negligible incidence of peptic ulcers in psychotics.

The observation that other psychosomatic and/or so-called "histamine" implicated states, i.e., asthma and hay fever, improved either with a pregnancy<sup>23, 24</sup> or with the onset of a psychosis,<sup>25-27</sup> suggested some common endocrine intervention. It was also noted that these allergic phenomena had an extremely low incidence among hospitalized psychotics.<sup>27-33</sup>

An early experimental observation of tremendously high "histaminolytic" or, more precisely, histamine antagonist titres in pregnancy—as shown by administration of 96 mg. of histamine base to a pregnant dog without adverse effects—was confirmed by the literature at that time,<sup>34-36</sup> and has since been reported by other workers.<sup>37, 38</sup> This suggested that certain common factors might be operative in both pregnancy and certain psychoses, and that this mechanism might involve adrenal participation.

The observations (1) that in general (but not always) the more severe the psychotic process—the higher the histamine tolerance; and (2) that higher histamine tolerance characterized hospitalized psychotics as compared with non-hospitalized psychotics, further implicated a connection between histamine-adrenal interaction and the psychiatric disorders under study.

The finding that both this interaction and the clinical conditions were influenced by sex steroids, thyroid and insulin, broadened the concept to suggest that some of the psychoses were metabolic disorders resulting from a histamine-adrenal-gonadal-thyroid (and, therefore, also pituitary) and possibly insulin imbalance; that the hormones of the adrenals, particularly of its

cortex, were in certain important essentials counterposed by what we have termed its antidynes — prominent among these being histamine, the sex steroids, insulin and thyroid.

## RESUMEN

Los autores evalúan la histamina como un agente bioquimioterápico en los trastornos psiquiátricos, y revisan los diversos experimentos que les indujeron a emplear la histamina: 1) el efecto causado por el paso de una corriente de choque a través de los tejidos vivos; 2) el elevado porcentaje de aclorhidria e hipoclorhidria en los pacientes psicóticos; y, 3) el aumento de la acidez gástrica causado por la terapia electroconvulsiva. Además, indican que otros investigadores psiquiátricos se interesaron, por otros motivos, en el uso de la histamina.

Los informes de diferentes investigadores sobre más de 500 pacientes psiquiátricos tratados mediante una u otra forma de bioquimioterapia histamínica, son prácticamente unánimes en cuanto a su reconocimiento del valor terapéutico de la histamina. El "porcentaje de mejorías" registrado, oscila entre el 24 por ciento (en el grupo de psicóticos hospitalizados por los autores) y más del 50 por ciento en otras comunicaciones. Se observa un porcentaje de mejoría más uniforme, de 50 a 60 por ciento, cuando se emplea la histamina junto con otros tratamientos.

La mejoría obtenida con la bioquimioterapia histamínica, como la han observado los autores, incluye la reducción de la ansiedad, depresión, irritabilidad, ensimismamiento, y conducta extraña, aumentando la viveza mental, actividad orgánica, higiene personal y relaciones personales. Los datos clínicos sobre la histamina indican:

1) que la histamina por sí sola constituye un tratamiento bioquimioterápico, tan eficaz como el ECT, en ciertos trastornos psiquiátricos; 2) que la resistencia a la histamina no indica resistencia a otros métodos terapéuticos, y que por el contrario, el tratamiento previo con histamina aumenta la eficacia de otros procedimientos, p.e. el ECT y el sub-coma insulínico; 3) que el empleo de tratamientos en serie, p.e. de histamina seguida de ECT o insulina, duplica el número de pacientes que obtienen una mejoría, y, en algunos casos, llegan a la convalecencia; 4) que las posibilidades de éxito son mayores cuanto antes se inicie el tratamiento; 5) que la bioquimioterapia por la histamina no produce los efectos secundarios indeseables del ECT y del coma insulínico, es más fácil de administrar y requiere menos aparatos especiales.

Se obtuvieron los siguientes datos biológicos importantes, al usar la bioquimioterapia por la histamina, estudiando la tolerancia a esta droga: 1) La tolerancia fué 50% mayor en los esquizofrénicos que en los psiconeuróticos; 2) aumentó con la gravedad de la enfermedad y la agitación del paciente; 3) disminuyó al dar esteroides sexuales y extractos de tiroides.

Los autores integran los datos fisiológicos y las observaciones clínicas ya mencionadas, con otros informes, tales como: 1) la relación directa entre los niveles histamínicos en la sangre y la profundidad del coma insulínico; 2) la baja frecuencia de la úlcera péptica en los psicóticos, y la alta incidencia de la aclorhidria e hiperclorhidria; 3) el hecho de que los estados psicósomáticos y/o los llamados estados "histamínicos," mejoran durante el embarazo o con la aparición de la psicosis; 4) la proporción tan baja de los estados alérgicos en los psicóticos hospitalizados; y, 5) las concentraciones histaminolíticas o histamino-antagónicas tan elevadas que se observan en el embarazo.

Algunas de las psicosis pueden ser trastornos del metabolismo, como resultado de un desequilibrio histamino-suprarrenal-gonadal, y, posiblemente, insulínico, siendo estas hormonas antidiabéticas, contrapuestas a las hormonas suprarrenales.

## RESUME

Les auteurs évaluent l'histamine comme agent biochimiothérapeutique dans le traitement des dérangements psychiatriques. Ils passent en revue les séries d'expériences et d'observations qui les ont conduits à l'emploi de l'histamine: (1) l'effet du passage d'un courant de choc à travers des tissus vivants; (2) l'incidence élevée de l'achlorhydrie et de l'hypochlorhydrie chez les sujets psychotiques, et (3) le haut degré d'acidité gastrique produit par la thérapie électro-convulsive. Ils signalent que d'autres investigateurs dans le domaine des recherches psychiatriques ont été également amenés à adopter l'histamine pour d'autres raisons.

Les rapports des divers investigateurs portant sur plus de 500 sujets psychiatriques qui ont reçu une forme ou une autre de biochimiothérapie à base d'histamine sont virtuellement unanimes au sujet de l'intérêt thérapeutique de l'histamine. Les "pourcentages d'amélioration" observés vont de 24% (dans la série des auteurs de cas psychotiques hospitalisés) jusqu'à 50% dans d'autres rapports; un pourcentage d'amélioration plus uniforme de 50-60% est observé lorsqu'on utilise l'histamine en combinaison avec d'autres thérapies. L'amélioration réalisée par la biochimiothérapie à base d'histamine, telle qu'observée par les auteurs, comprend la diminution de l'inquiétude, de l'abattement, de l'irritabilité, de la tendance au retranchement et à la singularité du comportement, et une amélioration de la vivacité, de la pensée, du fonctionnement, de l'hygiène personnelle et des relations avec autrui. Le dossier clinique relatif à l'histamine suggère les conclusions suivantes: 1) L'histamine employée seule constitue une biochimiothérapie non-convulsive pour le traitement de certains dérangements psychiatriques déterminés d'une efficacité égale à celle de l'ECT; 2) La résistance au traitement par l'histamine n'est pas une indication de la résistance à l'égard d'autres modes de traitement thérapeutique — au contraire, le traitement préalable par l'histamine augmente l'efficacité de certains autres traitements, entre autres l'ECT et l'insuline sous coma; 3) La mise en oeuvre de diverses thérapies en série, par exemple l'histamine, suivie l'ECT ou d'insuline, double le nombre de cas d'amélioration et de sujets entrant en convalescence dans certains groupes traités; 4) Plus le traitement est commencé tôt, plus grandes sont les chances de succès; 5) La biochimiothérapie par l'histamine est exempte des effets accessoires nuisibles de l'ECT et du coma par l'insuline, est facile à administrer et nécessite moins d'appareils spéciaux.

Des renseignements biologiques significatifs ont été révélés par la biochimiothérapie à base d'histamine, notamment en ce qui concerne la tolérance à l'égard de l'histamine qui: 1) est 50% plus forte chez les schizophrènes que chez les psychoneurotiques; 2) augmente avec la gravité de la maladie et le degré d'agitation; 3) est diminuée par les stéroïdes sexuelles et la thyroïde.

Les observations tant physiologiques que cliniques, qui ont été présentées ci-dessus, ont été intégrées avec d'autres données telles que: 1) la relation directe entre les niveaux sanguins d'histamine et la profondeur du coma d'insuline; 2) la très faible incidence de l'ulcère peptique chez les psychotiques, ainsi que la très forte incidence d'achlorhydrie et d'hypochlorhydrie;



3) l'amélioration des conditions psychosomatiques et/ou des conditions dites impliquées par "l'histamine" lors de la grossesse ou du début d'une psychose; 4) l'incidence extrêmement faible des conditions allergiques chez les psychotiques hospitalisés; 5) les titres histaminolytiques ou histamine-antagonistes extrêmement élevés dans les cas de grossesse — tous ces rapprochements tendant à prouver que certaines des psychoses peuvent être des dérangements métaboliques provenant d'un déséquilibre histamine-surrénal-gonadal-thyroïde et éventuellement d'insuline, et que ces hormones sont des antidynes faisant contrepois aux hormones des capsules surrénales.

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# An Appraisal of the Current Status of Sex Steroid Biochemotherapy in Psychiatry

## PART III

### ENDOCRINOLOGIC ORIENTATION TO PSYCHIATRIC DISORDERS

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Experimental findings and clinical observations in our histamine<sup>1-5</sup> and related studies<sup>6, 7</sup> suggested that alterations in endocrine patterns, particularly in respect to changes in adrenal cortical function, might be related to the etiology and pathogenesis of a number of major psychoses and to the psychotics' response to biochemotherapy. It was, therefore, decided to investigate the clinical and biochemical effects of different steroid hormones and related substances on schizophrenic, manic-depressive and involutional psychotics. The series selected for screening were the anabolic sex steroids, testosterone and estradiol;\* two recently synthesized steroids, pregnenolone and acetoxypregnenolone, and the cortical steroids. To date, most promising therapeutic results and theoretic implications have been derived from the studies on the sex steroids. The details of these steroids investigations will be presented in independent reports.<sup>8, 9</sup> The present communication is restricted to observation relating to a number of fundamental psychiatric perspectives gained through these studies.

#### HISTORY OF SEX STEROIDS IN PSYCHIATRIC THERAPY

Early efforts to arrest the malignant process of dementia praecox by use of sex hormone therapy date back to 1926. Kanders<sup>10</sup> claimed improvement in four of eight male patients given fifteen to twenty times the "usual dosage" of "male and female gonad extracts" over a period of months. Sippl<sup>11</sup> stated that he achieved improvement by transplanting healthy ovarian tissue into 6 dementia praecox patients. Kresztes,<sup>12</sup> the following year, reported favorable results following administration of testicular extract and related the greatest improvement to cases of least duration. Elsewhere, antuitrin-S was tried and though improvement was claimed,<sup>13</sup> the authors stated they could not exclude the possibility of spontaneous remission.

As the uncertain and low potency gonadal extracts were displaced by the crystalline sex steroids, the therapeutic application of what is now considered low dosage levels of these potent endocrines resulted in contradictory findings in psychiatric disorders.

Though attempts with female sex hormone therapy utilizing amniotin,<sup>14</sup> theelin (estrone),<sup>15-24</sup> estradiol,<sup>28-33, 19, 24</sup> stilbestrol,<sup>34, 35</sup> and progesterone<sup>36, 37</sup> were reported to be beneficial in many

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instances,<sup>14-17, 19-22, 32, 34, 24, 26-37</sup> they were described as ineffective by several cautious investigators.<sup>18, 23, 25, 33</sup>

In 1938, testosterone was administered to 5 male involutional melancholics by Barahal,<sup>38</sup> who found no improvement after 3 to 4 months of treatment with 10 mg. of the propionate given intramuscularly three times weekly. Two years later, he reported<sup>39</sup> that 7 overt homosexual psychotics with physical signs of gonadal insufficiency also showed no change in mental condition after receiving 25 mg. of testosterone propionate three times a week for 18 weeks.

Since 1940, the literature on testosterone therapy, part of which will be reviewed here,<sup>40-44</sup> shows more favorable results in a few studies, most of these on small numbers of patients. Guirldham,<sup>40</sup> in Britain, reported marked improvement in 4 male psychotics treated with testosterone propionate and androsterone benzoate. Pardoll and Belinson<sup>41</sup> administered 10 mg. of testosterone propionate twice weekly to 11 male involutional patients and concluded, after only one was discharged, that the results did not warrant routine use of testosterone. Zeifert<sup>42</sup> administered 25 mg. testosterone propionate twice daily for 20 days, 10 mg. twice daily for 10 days and half that dose for 10 days. Four of 5 male patients showed marked improvement though only 2 maintained the improvement.

Danziger and Blank<sup>43</sup> reported recovery in 3 of 5 males with involutional melancholia given 25 mg. of testosterone three times weekly for at least 12 weeks and remarked that "the patients who recover do so as if they were responding to the hormone . . . as if they were receiving specific therapy. It is possible that such cases, although clinically identical with those who fail to recover, differ from the others in some subtle way yet undiscovered." In a subsequent test, Danziger et al<sup>44</sup> did not achieve comparably good results.

Hoskins and his co-workers<sup>45-48</sup> reported on several aspects of testosterone therapy in the psychoses. Their first patient was a schizophrenic with a 35-year history of homosexuality. Endocrine therapy gave no results.<sup>45</sup> The following year, however, Rosenzweig and Freeman<sup>46</sup> reported on a series of 20 male schizophrenics. In addition to 25 mg. testosterone propionate daily, 10 patients were given 1 gm. of desiccated thyroid and 300 units A.P. gonadotropin. The effects of the sex hormone were discernible by comparison with the 10 control patients who received thyroid alone. The observers noted a better social adjustment and amelioration of symptoms.

A hypogonad male patient treated with methyltestosterone in dosages ranging from 10 mg. three times a week to 10 mg. three times a day for approximately 10 weeks was discharged in "apparently complete restitution."<sup>47, 48</sup> In a further study on 40 patients administered 25 mg. testosterone intramuscularly 3 times weekly for 6 weeks, the investigators found encouraging improvement in over 50 per cent of the cases. They reported that the patients became more alert, approachable and warm in their personal relationships but did not show really impressive change. Psychological studies revealed that the psychotic mechanisms were retained but under "materially better control."<sup>48</sup>

More recently, Altschule and Tillotson<sup>49</sup> stated that ECT produced effects similar to those following administration of steroid hormones, and listed these as: (1) fall in plasma protein levels, (2) fall in lymphocytes and eosinophiles, (3) increased diuretic response to water, (4) extracellular retention of water and sodium.

They attempted to duplicate the beneficial effects of ECT with desoxycorticosterone and with progesterone but reported inability to induce a remission in mental symptoms. Testosterone was then tried because of its marked anabolic action and a course of 50 mg. of the propionate was given daily for 2-3 weeks. Although detailed comparison and analysis of their data is not possible on the basis of published material, the therapeutic results were striking in that 11 of 17 patients on testosterone alone were reported as discharged, as were all 7 patients treated with testosterone followed by ECT. They believed that testosterone and ECT had effects which seemed interchangeable, and suggested that ECT benefits by increasing production of "some steroid hormones."

The authors' studies with different steroids have been presented in detail elsewhere.<sup>8, 9</sup> For the purposes of this report which is concerned primarily with biologic findings as they bear upon current psychiatric perspectives, it suffices to state that convalescent status rates of 86 per cent, 53 per cent and 30 per cent in, respectively, younger patients, psychotics with shorter hospitalization and the over-all uncategorized series were attained with combined massive dosages of testosterone and estradiol. Therapy was administered to a series of 40 hospitalized patients with schizophrenic, manic-depressive and involutional psychoses.

#### WHAT SIGNIFICANT BIOLOGIC DATA HAS TESTOSTERONE-ESTRADIOL BIOCHEMOTHERAPY REVEALED?

Five significant findings of our sex steroid studies are presented here for discussion. The detailed data of the laboratory phases of the study are embodied in separate papers.<sup>8, 9</sup>

1. *Marked increase of eosinophile cells* during the course of therapy was found in 14 of 15 of our patients receiving combined sex steroids. A gradual return to the lower levels was found after therapy was discontinued. In those patients attaining convalescent status, there appears to be a higher ratio between peak resting level of eosinophiles during or immediately following testosterone-estrogen therapy and the average resting level before treatment ("DEC Prognostic Index") than in those who showed no improvement.<sup>9</sup> (Table I, Fig. 1.)

It is interesting in this connection that the Scandinavian worker, Finn Rud<sup>30</sup> (in his study on "Eosinophile Count in Health and Mental Disease") considered an increase in eosinophile count as a favorable prognostic sign in certain forms of mental disease, particularly in the manic-depressive and what he referred to as the "constitutional" psychoses.

2. *The lymphocyte-neutrophil (L/N) ratio* changes in our patients receiving combined sex steroid therapy also suggest an inhibition of adrenocortical activity. A shift toward higher so-called "Addisonian ratios" was found to occur following testosterone-estradiol therapy. The most marked increase in the L/N ratio occurred in patients attaining improvement and convalescent status, possibly indicative<sup>31</sup> of greater inhibition of adrenocortical effects.

3. *Glucose tolerance determinations* (Exton-Rose procedure) were made conjointly with eosinophile counts before, during and after the course of therapy. Alterations in the eosinophile level referred to above were noted. Of the 15 patients, 11 or 75 per cent revealed tolerance curves described as "diabetic-type" in the literature. However, no clear or consistent pattern of change in the blood sugar level curves during, or after, therapy has as yet been noted.

4. Patients given testosterone-estradiol therapy seem to show reduced tolerance for histamine

TABLE I—CORRELATION OF IMPROVEMENT WITH DEC "PROGNOSTIC" INDEX

Patient		Age	Diagnosis	Total Dosage T/E in mg.	Results T/E Therapy	Dec Index
No.	Sex					
1	2	3	4	5	6	7
130	F	20	S.-c.	1300/43.3	++++	36.7
126	F	30	S.	1100/36.6	++++	25.0
133	F	23	S.-s.	800/26.6	++	14.4
216	M	53	M.D.-d.	1450/76.6	++	13.6
128	F	56	M.D.-d.	800/26.6	++++	11.0
218	M	34	S.-p.	1250/41.8	++++	10.2
113	F	51	M.D.-d. Inv.	487/31.6	++++	7.1
131	F	29	S.-p. P.P.	1100/36.6	0	5.9
211	M	46	S.-p.	1250/41.7	0	5.2
212	M	62	M.D.-m.	1300/43.3	0	5.1
127	F	17	S.-p.	750/33.2	(++++)*	3.1
125	F	30	S.-c.	1125/33.2	+	3.1
213	M	56	M.D.-m.	1200/36.6	(+)*	2.9
129	F	34	S.	900/31.6	+	2.7
214	M	53	I.M.-p.	1150/36.3	0	1.7
134	F	53	I.M.-p.	750/38.3	0	1.4
135	F	47	I.M.	1050/61.6	0	0.92
S. — Schizophrenia				M.D.-d.	— Manic-Depressive, depressed	
S.-s. — Schizophrenia, simple type				M.D.-m.	— Manic-Depressive, manic	
S.-c. — Schizophrenia, catatonic type				M.D.-d. Inv.	— Manic-Depressive, involution	
S.-p. — Schizophrenia, paranoid type				I.M.	— Involutional Melancholia	
( )* — Transient				I.M.-p.	— Involutional Melancholia, paranoid	
DEC — Ratio of peak resting level during or after				P.P.	— Post-partum	
course of treatment to average of resting				++++	— Attainment of Convalescent Status	
levels before treatment						

After Sackler et al: *Acta Psych. et Neurol.* (8), *Proc. Soc. Exper. Biol. & Med.*, (9).

when compared to previous dosages tolerated when they had been on histamine alone. This has been referred to in the preceding paper. It is possible that this reduced tolerance is further evidence of the antidyne, or opposing, action of the sex steroids to adrenocortical hormones, perhaps the result of: (1) an inhibition of adrenal cortical activity, or (2) a "binding" or "neutralization" of adrenal hormones, and/or (3) a counter-effect at the end-organ elements.

5. *Correlation of side-actions* of testosterone-estrogen with psychiatric effects revealed that patients who attained the greatest improvement showed the greatest number of side-actions, e.g., hirsutism, hoarseness, perineal engorgement and edema. Patients failing to improve may be considered more severely ill; these show greater tolerance for the sex steroids even as increased tolerance to histamine appears related and proportioned to severity of illness.

In those patients refractory to therapy, it is possible that certain substances counteractant to the sex steroids (and to histamine) are present in a greater operative concentration than could be overcome with the dosages of sex steroids administered to these patients.

#### WHAT IS THE CHARACTER OF THE CLINICAL IMPROVEMENT WITH TESTOSTERONE-ESTRADIOL BIOCHEMOTHERAPY?

Improvement,\* when achieved, is usually first reported as a physical feeling of well-being, relaxation and improved sleeping. In some patients, the response is dramatic and as though

\*The improvement as noted on psychological testing is reported in Part IV.

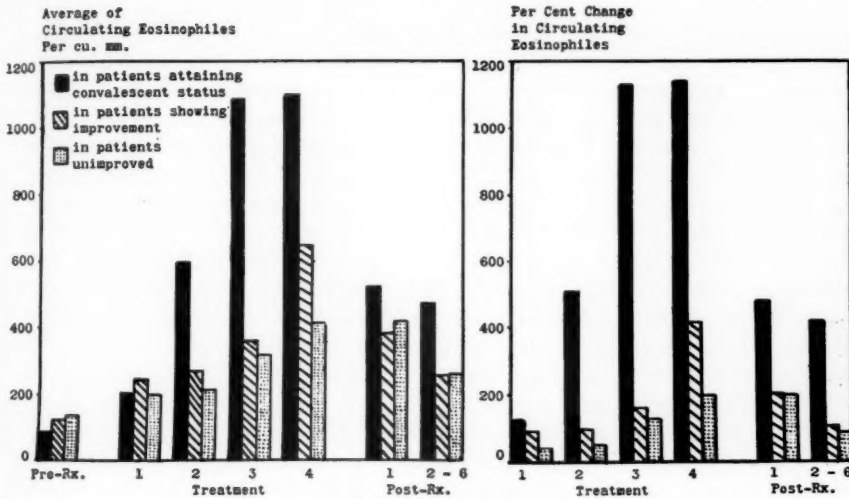


Fig. 1. Eosinophilia in sex-steroid-treated psychotics.  
After Sackler et al: *Proc. Soc. Exper. Biol. & Med.*, (9).

produced by a specific therapeutic agent. In others, it is gradual but definitive.

Improvement in affect, lessening of depression and increased interest and activity follow the feeling of well-being. The patients show more attention to personal hygiene and dress, become more alert and function more efficiently.

Later, thinking becomes clearer and association and stream and content of thought more normal, delusional ideation disappears, and ability to concentrate, judgment and insight improve.

#### THE UTILIZATION OF PITUITARY AND ADRENAL HORMONES AND RELATED STEROIDS IN PSYCHIATRIC THERAPY

In 1938 and 1940, prior to the development of highly concentrated extracts and the availability of the active principles of the adrenal cortex, 1 cc. of an adrenal cortical extract was administered daily and encouraging responses were claimed by Loehner,<sup>52, 53</sup> in dementia praecox and in manic-depressive psychoses, in the manic phase. He believed there was a "striking similarity in both symptoms and signs of hypoadrenalism and . . . dementia praecox." T. V. Moore<sup>54</sup> used a similar extract in the treatment of 24 manic-depressive psychotics and claimed that more than half were discharged within six months as compared to only 4 of 48 control patients.

In 1943, Guiridham<sup>55</sup> reported a psychotic patient with "dyspituitarism" who responded dramatically to a pituitary extract (Preloban).

In 1941, and again in 1943, Haynes and Carlisle<sup>56, 57</sup> treated schizophrenia with desoxycorticosterone acetate, 5 mg. in 1 cc. oil intramuscularly, and reported that the patients became more relaxed, cooperative and interested. Their rationale was: (1) to raise the blood pressure and effect improvement in brain metabolism, (2) to help achieve a "normal glycogen lactic acid

cycle" by restoring normal cerebral carbohydrate metabolism, and (3) to relieve hyperpotasemia. They concluded that it was not a "cure-all," but that it had a more rational basis than ECT and was safer. Evidence on the relationship of the administered desoxycorticosterone to cerebral carbohydrate metabolism was not presented.

In 1949, Jens<sup>58</sup> reported that desoxycorticosterone acetate given in a dosage range increased progressively from 5 mg. to 35 mg. weekly achieved "recovery" in 4 of 16 schizophrenic, manic-depressive and involutional melancholic patients. More recently, Cranswick et al<sup>59</sup> described their results following therapy with desoxycorticosterone and ascorbic acid of 45 patients—schizophrenic, manic-depressive, depressed and manic. A dosage of 3 mg. desoxycorticosterone was described as optimal while larger amounts (10 mg.) were noted to be depressing.

A number of reports have appeared<sup>60-63</sup> on the physiologic effects of concentrated adrenal extracts, the newly synthesized Compound E and ACTH on psychotic patients. The occurrence of lymphocytopenia and eosinopenia is specifically characteristic of the effect of the glucocorticoid fraction of the cortical hormones (Compound E) and also usually follows administration of ACTH. This effect, among others, is also produced by ECT.<sup>51, 64-66</sup> A number of workers have anticipated that beneficial therapeutic clinical results would follow the use of these substances. However, we are not as yet cognizant of any report of definite and sustained clinical recovery in specific psychiatric disorders as a result of ACTH or cortisone treatment. In fact, quite the contrary seems to have occurred, for the administration of ACTH, cortisone and potent adrenocortical extracts has been followed by psychotic manifestations in a number of hitherto clinically non-psychotic subjects.<sup>67-69</sup> Such an eventuality was predicted on theoretical grounds in two of our previous publications.<sup>6, 7</sup> It is surprising and disappointing that no detailed studies on such significant—even though untoward—results have as yet found their way to publication. If these substances do produce or activate psychoses, then they and all related compounds must be carefully appraised as to their neuropsychiatric effects by competent psychiatric clinicians and investigators. Patients receiving these compounds should be studied psychiatrically prior to institution of therapy, throughout the course and after its completion. In principle, potent metabolic preparations should not be released for general use until their effects upon cerebral function are definitively ascertained.

## RESUMEN

Teniendo como base los informes experimentales obtenidos, y las observaciones clínicas que llevaron a los autores a relacionar las alteraciones en las constelaciones endocrinas, especialmente en la función córticosuprarrenal con la etiología y patogenia psiquiátricas se investigó el efecto clínico y bioquímico de las diferentes hormonas sexuales administradas a pacientes esquizofrénicos, maniaco-depresivos, y psicóticos evolutivos.

En los recientes artículos de Altschule y Tillotson se revisa la historia de los esteroides sexuales en la terapia psiquiátrica desde 1926. Las observaciones clínicas de los autores, revelan que los pacientes jóvenes, los psicóticos con períodos cortos de hospitalización y los no clasificados, en general, tratados con grandes dosis combinadas de testosterona y estradiol, presentaron mejorías de un 86 por ciento, 53 por ciento y 30 por ciento, respectivamente. Este informe se



refiere principalmente a los resultados biológicos que obtuvieron durante esta terapia, y que incluyen: 1) Un aumento notable de los leucocitos eosinófilos, durante el tratamiento de 14 de los 15 pacientes estudiados. Se halló que el aumento de los eosinófilos en el recuento directo estaba relacionado con la mejoría clínica, puesto que se obtuvieron recuentos más elevados de eosinófilos en los pacientes que habían mejorado hasta llegar a la convalecencia; 2) la proporción entre linfocitos y neutrófilos (L/N) tendió a aumentar, sugiriendo también una inhibición de la actividad córticosuprarrenal, observándose también el aumento más notable en la proporción de eosinófilos en los pacientes que habían llegado a la convalecencia; 3) las determinaciones de la tolerancia de glucosa (método de Exton y Rose) dieron curvas clasificadas de "tipo diabético" en un 75 por ciento, o sea en 11 de los 15 pacientes. No obstante, no se presentó un cambio considerable en la curva o nivel de la glucosa sanguínea; 4) En relación con las dosis toleradas anteriormente, los pacientes sometidos al tratamiento combinado de esteroides sexuales mostraron aparentemente una tolerancia menor a la histamina. Este resultado estuvo también relacionado con una acción fisiológica antagónica de las hormonas córticosuprarrenales; antagonismo que se considera como el llamado efecto antidina.

Mientras que otros investigadores creían que con el empleo terapéutico de estas sustancias en la esquizofrenia, se obtendrían resultados satisfactorios, los autores profetizaron que la administración de ACTH, cortisona, y extractos concentrados córticosuprarrenales, iría seguida de manifestaciones psicóticas en un número considerable de casos clínicamente considerados no psicóticos. Basados en datos teóricos, los investigadores previeron esta posibilidad en dos de sus publicaciones anteriores.<sup>6, 7</sup> En relación con los efectos neuropsiquiátricos, los autores insisten en que, si estas sustancias producen o activan una psicosis, tanto éstas como todos los compuestos con ellas relacionados, deben ser cuidadosamente valorados por psiquiatras clínicos e investigadores competentes.

Los pacientes tratados mediante estos compuestos deben ser estudiados psiquiátricamente antes, durante y después del tratamiento. En principio, generalmente, las preparaciones metabólicas concentradas no deben ser empleadas hasta que hayan sido determinados definitivamente sus efectos terapéuticos sobre las funciones cerebrales.

#### RESUME

Sur la base d'observations cliniques et de conclusions expérimentales qui les ont conduits à mettre en corrélation les types endocrines, particulièrement en ce qui concerne la fonction surrénocorticale, avec l'étiologie et la pathogénie, les auteurs ont fait une enquête sur les effets cliniques et biochimiques des hormones différents de stéroïdes sexuelles sur les psychotiques schizophrènes, maniac-dépressifs et involutionnels.

L'article passe en revue l'historique des stéroïdes sexuelles dans leurs applications à la thérapie psychiatrique depuis 1926, se basant sur les récents rapports d'Altschule et de Tillotson. Les observations cliniques des auteurs, qui sont présentés ailleurs,<sup>8</sup> ont révélé la réalisation d'une amélioration respectivement dans 86% des cas pour les sujets jeunes, 53% des cas pour les psychotiques avec courte hospitalisation, et 30% des cas pour l'ensemble des groupes non classées, et cela pour des dosages massifs combinés de testostérone et d'estradiol. Le présent

rapport a surtout trait à leurs observations d'ordre biologique pendant l'application de cette thérapie. Ils ont constaté notamment: 1) Une augmentation marquée des éosinophiles a été observée pendant le cours de la thérapie chez 14 sujets sur un total de 15 cas étudiés. L'accroissement en éosinophile, constaté au dénombrement direct, a coïncidé avec l'amélioration clinique des cas; 2) Le rapport lymphocyte-neutrophile (L/N) a tendu vers des valeurs plus élevées, suggérant également une inhibition de l'activité surrénocorticale. Ici aussi, on a constaté que l'augmentation la plus forte de ce rapport était observée chez les sujets entrant en convalescence; 3) La détermination des degrés de tolérance à l'égard du glucose (mode opératoire Exton-Rose) a donné des courbes qualifiées de "types diabétiques" dans 75% des cas, soit chez 11 sujets sur un groupe de 15 cas étudiés. Toutefois, on n'a pas observé de modification uniforme du niveau ou courbe du sucre dans le sang; 4) Les sujets auxquels on a appliqué une thérapie combinée à base de stéroïdes sexuelles ont semblé manifester une réduction de tolérance à l'égard de l'histamine par rapport aux doses antérieurement tolérées. Cette constatation a été aussi apparentée à une action physiologique antagoniste aux hormones surrénocorticales, un antagonisme désigné sous le nom d'effet antidyne.

Alors que certains investigateurs avaient prévu qu'on obtiendrait des résultats salutaires par l'emploi thérapeutique de ces substances en schizophrénie, les auteurs avaient prédit que l'administration d'ACTH, de cortisone et d'extraits surrénocorticaux efficaces se traduirait par des manifestations psychotiques dans un nombre significatif de sujets cliniquement non-psychotiques. Ces investigateurs avaient mis en garde contre cette éventualité sur la base de raisons théoriques dans deux de leurs publications antérieures.<sup>6,7</sup> Ils font remarquer que "si ces substances produisent ou activent des psychoses, il convient de les faire évaluer avec soin, ainsi que tous les composés dérivés, pour ce qui est de leurs effets neuropsychiatriques, par des cliniciens et des investigateurs psychiatriques compétents. Les sujets auxquels on administrera ces composés devront être examinés au point de vue psychiatrique avant de leur appliquer cette thérapie, au cours de sa mise en oeuvre et après sa cessation. En principe, les préparations métaboliques de grande efficacité ne devront pas être mises dans le commerce pour l'emploi courant avant qu'on ait déterminé avec précision leurs effets sur la fonction cérébrale."

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# Improvement in Schizophrenics Following Histamine and Steroid Therapy as Revealed in Psychological Tests

## PART IV

### ENDOCRINOLOGIC ORIENTATION TO PSYCHIATRIC DISORDERS

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In this study, psychological tests were used as a supplementary diagnostic procedure and as one of the gauges of the effectiveness of therapy. The test battery usually included the Wechsler-Bellevue, Rorschach, Thematic Apperception, Bender Gestalt and Figure Drawings. These tests were used in accordance with the needs of the patients. The corroborative evidence of the battery aided in the evaluation of the total picture, and highlighted diverse personality features. Among the projective methods, the Rorschach made a signal contribution in the description of personality dynamics and the processes of retardation and distortion in growth.

A comparison of test findings before and after therapy often confirmed the clinical evaluation and delineated those areas in which there had been improvement. Repeated testings demonstrated favorable changes in improved schizophrenics frequently without essential modification in the core of the personality. Changes in these patients have often been as erratic and unpredictable as the course of the disease itself. The problem of evaluation of personality change often eludes specific quantitative criteria. The schizophrenic personality structure is deviant, uncoordinated and unbalanced. When the pathological exaggeration or reduction of significant psychic factors moves in the direction of the more "normal" or usual course of development, such modification is considered to be of a positive nature. These changes in psychological phenomena must be regarded within the framework of the total economy of functioning and the interrelationship of all the personality components.

Preliminary examination of pre- and post-therapy test productions suggests several areas most susceptible to modification. There is of necessity some overlapping, but schematically, they may be arranged thus: (1) intellectual functioning, (2) productivity, (3) associational thought content, (4) relation to reality, (5) fantasy, (6) emotional functioning, (7) anxiety, (8) aggression and passivity and (9) attitude to the disease.

In terms of intelligence, improved schizophrenics frequently show a more optimal effectual functioning. Rational control becomes more efficient with fewer bizzarities and a less alien thought content. Conformity strivings may increase and provide an anchorage for some patients who tend to live largely in a world of their own creation. A mental approach which emphasizes details that ordinarily escape notice may give way to a healthier interest in the

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prosaic and the mundane. In this respect the intellectual functioning is closely related to the grip on reality. The schizophrenic may show distortion varying from a painfully meticulous exactitude to general looseness and disorganization. Associational productivity previously inappropriately high becomes more realistically geared with reduced ambition. On the other hand, a scant and meager productivity, after re-testing, often reveals a release of psychotic blocking and diminished fragmentation of the thought processes.

Changes in the fantasy reflecting the total sum of productive efforts moves in the direction of the more normal. When there had been too much fantasy, when the patient lived estranged from the community, immersed in his own autistic imagination, improvement was recognized when these energies were deflected into more creative reality-oriented activities. When blocking had restricted the fantasy, post-therapy testing may show greater activity in this area with autism giving way, in some patients, to constructive imaginative productions. The *dramatis personae* of the fantasy life also provide clues to dynamic changes in the intensity and handling of aggressive impulses. In some situations, a primitive, easily-discharged hostility is reduced. In others, resignation and apathy are exchanged for more positive, socially-acceptable aggressive attitudes.

The emotional functioning of biochemically improved schizophrenic patients often reveals, after re-testing, tentative groping toward affective contact—sometimes timid, often precarious. However, these efforts do make an inroad into the withdrawal and strong sense of detachment and isolation. Affective lability and regressive explosive outbursts may also be reduced and trends toward more mature constraint in social adaptation emerge. The schizophrenic's anxiety is a typical one. He apparently recognizes with singular insight, the malignancy of the deteriorative process within. His test productions often show with amazing clarity how deeply he suffers from a diffuse awareness of impending catastrophe. Post-therapy testing has revealed in some improved patients an alleviation of this anxiety to the point where they can function on a more comfortable level. The individual may cope with his illness more efficiently. The depressive load is lifted, the sense of futility is less marked. This is often closely associated with modifications in other areas where gruesome images, feelings of isolation, and the cold, cadaverous quality of the test productions are exchanged for more pleasurable, less morbid preoccupations.

Two case illustrations may demonstrate the dramatic change that post-therapy testing has revealed in several of our patients.

#### CASE ILLUSTRATION I—HISTAMINE BIOCHEMOTHERAPY

*Clinical Status at Time of First Test:* This 28-year-old woman, a commercial artist, came for psychiatric consultation because of palpitations and hand tremors. She dated the beginning of these symptoms to almost a year previously when she experienced, with each onset of her menses, the sensation that her blood was draining into her feet. She complained of nocturnal anxiety attacks with much shivering and shaking and a shrinking sensation in her abdomen, described as "a feeling of fright as if someone you love is about to be injured." These attacks increased in intensity without perceptible motivation. She also complained of a tightening sensation over her chest, back of her neck and shoulders. She refused sexual relations with her husband because of her conviction that it would lead to heart disease. Depression set in with suicidal tendencies which became increasingly pronounced. She was diagnosed as a schizophrenic after clinical study and was placed on histamine therapy after pre-treatment testing was completed.

*Psychological Findings of First Test:* The first Rorschach displayed as a major feature, this patient's primitive emotional explosiveness. She was on the one hand extremely stereotyped, but her irrational thoughts, and bizarre thought content revealed how far removed she was from reality. She had thus far defended herself against the foreign nature of her thoughts by repeating to herself and to others that she was an artist. This defense was crumbling and she was unable to utilize these feelings in the formulation of creative productions. Her anxiety, tension and depression were marked and in some measure associated with an awareness of her disabled controls. She seemed like an impotent spectator awaiting the inevitable disaster against which she could neither protect nor defend herself. Her sense of futility was keen and she seemed ready to succumb to the deteriorative forces within. Her sexual feelings and thoughts were colored by destructive impulses. They precipitated so much anxiety that she withdrew from situations that might evoke them. Her Thematic Apperception Test stories also showed inappropriate affect, isolation and an inability to experience and maintain close emotional ties. Picture 13MF, a scene that frequently elicits heterosexual fantasies, was described as "a man who killed a woman in a rage because of love." A blank card, that often evokes deeply personal material was seen in a detached way, "If I were to sketch and just to sketch, I would sketch flowers because I'm best at that. I would merely make a line-drawing. It would have no meaning except for the pleasure of drawing because I love line and motion more than I love color. I see this as black and white."

Her figure drawings were stylized heads. They were quite grandiose in size but revealed a debilitating anxiety. The quality of her pictures was one of emotional coldness. Her inability to complete the body below the neck apparently reflected a defect in self-image and an unwillingness to meet problems centered about the body area of sexuality.

The total test findings patterned out a schizophrenia. The process was becoming increasingly acute and the defenses were rapidly breaking down. Her situation was a precarious one.

*Clinical Status at the Time of Second Test:* In the interval between tests the patient had received a four-week course of histamine. Changes in clinical symptoms included improved sleeping habits, a reduction in the frequency of anxiety attacks and a lessening of the depression. Her functioning at home and in work was improved. Evidences of emotional lability, though still present, were less intense. The difficulty in her marital relations persisted.

*Psychological Findings of Second Test:* Her emotional lability reappeared, but in more diluted form in the second Rorschach. Precarious controls were being established and her fear of being victimized by her emotions was reduced. Her tension, depressions and the acute anxiety about her condition also showed some alleviation. Her productions reflected elements of creativity and artistic sensitivity rather than unmodified sensation and emotion. She could permit herself to be imaginative without being bizarre and attempted to handle her thoughts and feelings in keeping with the reality elements of the situation. Her sexual impulses still constituted a threat but this sphere of her functioning seemed generally less painful to her.

The figures on the Thematic Apperception Test were somewhat less detached, but still suggested difficulty in experiencing warm emotional ties. In some instances, abstract ideation gave way to more prosaic preoccupations. The depressive feelings of despair, the loneliness and isolation, the fear of being engulfed by her emotions, the anxieties and sexual difficulties were generally less pervasive. The 13MF picture was described as one in which "both partners were spent" but still as "slightly repulsive." She added, "I don't get the feeling of murder like I did last time." The blank card elicited a more sympathetic association than on the first test. "I see a very lovely sunny room. Something made me think of a man and woman in an embrace. Along with the picture I get a feeling of security—of an understanding love. It's something lighthearted and has a feeling of fun about it."

In contrast to the stylized portraits of the first test, the patient now drew more complete figures. The woman was nude, graceful in line and sexually appealing. Insecurity persisted in the absence of footing and schizoid elements were again emphasized in the traces of body narcissism and self-immersion. The male figure was fully clothed and seemed more cordial. A significant feature of the drawing was her inability to find a position for his right forearm and hand, and her final decision to omit them. Thus, though she was a trained artist and drew with assurance, certain areas caused sufficient difficulty to result in a castrated figure.

In sum, the findings of the second test revealed an arresting of the schizophrenic process that previously showed signs of becoming increasingly acute.

*Clinical Status at Time of Third Test:* Six months after the first test and 8 months after the initial examination, this patient was given a third series of tests. During this 6 month interval she had been placed on maintenance histamine therapy three times a week. For a two-week period, she was off therapy and then it was resumed on a three times a week maintenance basis.

Her clinical status at this time showed continuing general improvement. She was less able to achieve relationships than she believed, and her description of the existing anxiety still had a psychotic quality, but she

functioned more satisfactorily at home and at work. Her situation was no longer acute. Her sleeping habits were improved and the palpitations and tremors were no longer present. The depression was reduced and suicidal tendencies had entirely disappeared. Her relationship with her husband was further improved. Her sexual life was more satisfactory than it had been and she achieved orgasm frequently.

*Psychological Findings of Third Test:* On the third Rorschach test this patient showed a considerably strengthened control with an emphatic diminution of the previously violent affective outpourings. The reduction in lability was accompanied by a more positive feeling tone. Her autistic fantasy was also reduced and her grip on reality more firm. Her anxiety exerted a less constraining effect on her functioning. On the third Thematic Apperception Test, her characters appeared in more intimate domestic situations with reduced aggressive content. She showed greater spontaneity and less ennui. Her fantasies reflected less malice and hostility. However, in the body image reflected in the third set of drawings she showed some reversal in comparison with the improvement revealed in the second test. The female figure lost her face. The patient still recognized the importance of the "self" and showed a drive to social participation but seemed egocentrically blocked. The feet were now included, which suggested greater security in the environment. However, there were gaps in the body wall, indicating that she might not be as well insulated against the hazards of the environment as might appear on the surface. The male figure also showed some reversal in comparison with the second set of drawings in that he, too, had lost his face and his clothes, except for a pair of bathing trunks. While neither the male nor female figure were at the depressed level of the original drawings, they did show some loss of the gains revealed in the second test.

To recapitulate, during a period of eight months and three testings this patient showed positive though not totally consistent gains. Her emotional state was more controlled. Reality adaptation and interpersonal relationships appeared more satisfactory and she had gained a considerable measure of relief from her anxiety and depression. The third set of drawings showed some loss in terms of relation to reality not noted on the other tests nor in clinical evidence. The instances of peculiar thought content were diminished and less bizarre, but remained like persistent threads throughout her test productions in sufficient strength to stamp this as a schizophrenia. Compulsive mechanisms, especially noted in the second and third tests were apparently used successfully in her struggle against the disease. Perhaps the most gratifying finding in the last examination was the relative serenity which this woman enjoyed in contrast to her acute condition as projected in her initial productions.

#### CASE ILLUSTRATION II — SEX STEROID THERAPY

*Clinical Status at Time of First Test:* The patient is a 15-year-old boy. The chief complaint as described by the parents was that he had become unmanageable at home since the age of 13½. In the succeeding 18 months he had evidenced increasing behavior disorders. He was extremely abusive to the parents both verbally and physically. Other complaints which also appeared at the time of puberty included a craving for knives which he used on the household furniture, his reluctance to bathe and his isolation from the family's social life. Before the onset of these symptoms he had been described as a "very good child" but shy and unsociable. At first, the patient denied the existence of his symptoms and was extremely resentful of his parents to whom he attributed all his difficulties. He said the doctors were "paid agents of his father and mother." He later admitted that his grades had fallen off markedly at school and that he was "disinterested in things."

The medical history revealed an endocrine dysfunction. At the time of puberty the patient had been given anterior pituitary injections for a short period. Subsequently, he was given thyroid which he has continued taking to date. This was the boy at the time of the first testing and at the time steroid therapy was instituted.

*Psychological Findings of First Test:* The findings of the first Rorschach revealed extreme blocking. His total of three responses was inappropriately low and in itself constituted an index of a malignant disorder. Extreme rigidity, negativism and primary withdrawal were prominently indicated. One of his three responses was an oligophrenic detail, a reflection of the fragmentary thinking of the blocked psychotic. The record was completely barren, without savor and characterized by a lack of enlivening qualities, with a total absence of fantasy and affective response. His Thematic Apperception Test stories were also very limited and unrevealing. The content was bland, the language incredibly evasive. His figure drawings presented a contrast to his performance on the other tests in terms of the diligence of his application. Perfectionistic drives and compulsive exactitude were emphasized to an intolerable degree. He erased continually in his efforts to alter and perfect and showed a painful preoccupation with minute aggressive details. The drawings exuded a venomous hostility.

The extreme limitation of material and excessive blocking on the tests suggested a serious disorder. The depth of his withdrawal and emotional detachment was compatible with schizophrenia. Some evidence of mental impairment appeared in the fragmentation of thinking. Mechanisms of a compulsive nature apparently played an important role in his disturbance.



*Clinical Status of Second Test:* At the time of the second test, one month later, the patient had been given 20 sex steroid injections. His clinical status showed marked change in many areas of functioning. He was less unmanageable at home. His outbursts, though still in evidence, were diminished considerably both in frequency and intensity. He gained some insight and admitted some share of responsibility for the difficulties at home. Yet he continued to point to his parents, especially his mother, as a major source of irritation. There was appreciable improvement in his scholastic functioning. The hostility against the doctors was also reduced and he became more accepting of the treatment procedures.

*Psychological Findings of the Second Test:* On the second Rorschach, given after treatment, this adolescent's blocking was markedly decreased. He gave fourteen instead of three responses. The excessive rigidity was reduced and the conformity strivings strengthened. The record was less arid and showed some evidence of life. Two fantasy-dictated responses appeared, one healthy, one mildly autistic. Associational content was broadened and the boy showed faint stirrings in the affect that fitted harmoniously into the more favorable total picture. Although the Thematic Apperception Test stories were still limited, they were more specific, less bland and more active with a more hopeful and lively tone. The figure drawings also reflected some improvement. They were still perfectionistic and hostile, but the boy showed reduced anxiety and aggression, and was not as fanatic in his exactitude.

The findings of the second examination again revealed a seriously disturbed boy still largely removed and inaccessible. However, the increased productivity and the new evidences of life, together with the reduction of rigidity and negativism appeared as positive gains toward a more satisfactory adjustment.

### SUMMARY

Repeated psychological testings were used as an adjunct to the diagnostic and therapeutic procedures described in the other papers in this series. Since the projective methods frequently uncover material that is not always translated into observable clinical symptoms, they may provide an objective evaluation of the personality structure and the integration and patterns of ego functioning. Specific areas within the personality that have proven most susceptible to biochemotherapeutic change have been discussed and illustrated with two case histories.

### RESUMEN

Como un procedimiento complementario de los métodos diagnósticos y terapéuticos descritos en otras comunicaciones de esta serie, se han empleado repetidamente una serie de pruebas psicológicas. Como los métodos proyectivos permiten con frecuencia poner al descubierto un material psicológico que no siempre se traduce en síntomas clínicos observables, pueden permitir una evaluación objetiva de la estructura de la personalidad y de la integración y modalidades de funcionamiento del yo. Se examinan e ilustran, con dos historias clínicas, las áreas específicas situadas dentro de la personalidad, que han demostrado ser más susceptibles a los cambios bioquimioterapéuticos.

### RESUME

Des essais psychologiques suivis ont été utilisés comme complément des modes opératoires diagnostiques et thérapeutiques décrits dans les autres études de la présente série. Vu que les méthodes d'extériorisation révèlent fréquemment des renseignements qui ne se traduisent pas toujours par des symptômes cliniques observables, elles sont de nature à fournir une évaluation objective de la structure de la personnalité, ainsi que l'intégration et la détermination des types de fonctionnement du moi. Deux cas d'observations sont donnés à titre d'exemples pour préciser les zones au sein de la personnalité qui se sont montrées les plus susceptibles aux modifications biochimiothérapeutiques.

# On the Pathogenesis Of Certain Psychiatric Disorders

## PART V

### ENDOCRINOLOGIC ORIENTATION TO PSYCHIATRIC DISORDERS

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The first half of the 20th century marked the beginnings of psychiatry as a science, the second half of the century should mark its fulfillment. Current developments in the field of metabolism and in the biochemical approaches to psychiatric disorders give promise for the ultimate fruition of the science of psychiatry—a science which will enable us to predict, prevent, modify and control psychiatric disorders as a result of a definitive determination of specific etiologic factors and a clearer understanding of pathogenetic mechanisms.

Though a biochemical orientation toward certain major psychiatric disorders could have been based on a rich clinical heritage (Kraepelin), the half-century gap in neuroendocrinologic psychiatric developments following the early use of thyroid for the treatment of cretinism, may in a way, prove to be one of the saddest chapters in the history of cerebral physiology. The brilliant deductions and admonitions of Kraepelin, Jellgersma, Freud and, more recently, van Ophuijsen, that metabolic factors were fundamental to many of the psychoses, went unheeded and the opportunities afforded by modern biochemical advances were lost. As a result, more than a third of a century was lost, this period being generally marked only by sporadic, unsustained and unfulfilled attempts to approach fundamental psychiatric processes neuroendocrinologically.

For the past few years, our group has attempted to integrate experimental investigations with clinical observations and experiences. Efforts have been made to define neuroendocrinologic and biochemical findings, to establish sharp criteria for the evaluation of our new biochemotherapies, to explore the fundamental physiologic implications of our data, to constantly test all these elements in the light of long established clinical precepts and to venture some integrating formulations as to the etiology and pathogenesis of certain of the psychoses.

#### THE CLINICAL IMPLICATIONS OF THE NEWER BIOCHEMOTHERAPIES

The clinical data deriving from our studies in biochemotherapy suggest a number of significant points:

1. Early institution of biochemotherapy may eliminate the necessity for hospitalization for some patients and reduce hospital stay for other patients already hospitalized.

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2. If hospitals would add the newer biochemotherapies to their therapeutic armamentaria and promptly and regularly utilize *all* available procedures, they could at least double the number of patients leaving currently as a result of treatment.

3. An appreciable number of patients may be spared ECT and insulin coma and these procedures may be held in reserve for patients refractory to the simpler and probably more physiologic biochemotherapies.

#### BIOLOGIC FINDINGS RESULTING FROM SOME RECENT BIOCHEMOTHERAPEUTIC STUDIES; THEIR THEORETICAL IMPLICATIONS

More fundamental to our understanding and ultimate control of severe psychiatric processes are a number of our biologic findings which point significantly to the metabolic aspects of these disorders.\*

In respect to possible etiologic and pathogenetic factors, a number of these phenomena are, to say the least, provocative:

1. The group differences in tolerance to histamine reveal that psychotics as a group, have considerably greater resistance than psychoneurotics. This suggests the presence of a greater operative concentration of a histaminolytic substance in association with the psychotic process.

2. A greater ability to tolerate histamine was noted in hospitalized as compared to non-hospitalized psychotics, again suggesting the possibility of a rough correlation between severity of psychiatric disease processes under study and resistiveness to the effects of histamine.

3. Two of the biochemotherapies—the sex steroids and thyroid—appear to reduce the psychotic's resistance to histamine, implying a reduction of the quantity of operative circulating histamine-antagonist or antidyne substance following their use.

4. Ability to tolerate the sex steroids without, or with fewer, side-actions was most marked in hospitalized patients psychiatrically unresponsive to sex steroid therapy, considerably less marked in hospitalized patients improving on this therapy and least marked in non-hospitalized psychotics.

It is, therefore, suggested that physiologic counteractions (antidyne effects) between two groups of hormones or physiologic substances exist—the sex steroids, thyroid, histamine on the one hand, and a histaminic-antidyne substance on the other. An increase in the concentration of the sex steroids and thyroid seems to alter the operative effectiveness of the "histaminic-antidyne" substance in relation to histamine.

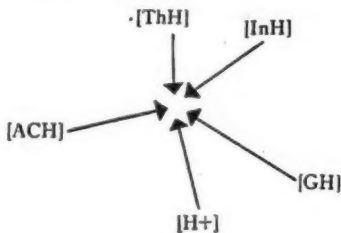


FIG. 1  
Schema of  
antidyne  
mechanisms.

\*Schizophrenic, manic-depressive and involutional psychoses.

5. So-called "diabetic-type curves" (by the Exton-Rose procedure) were determined in 75 per cent of our group of psychotics. Histamine appears to be capable of changing the character of this response in the direction of the more "normal" and, therefore, in this regard seems to act in an anti-adrenocortical manner or with an insulin-like effect.

6. Sex steroid therapy raised resting eosinophile levels with great uniformity—in 14 of 15 patients, with the greatest increase apparent in patients attaining improvement as was shown by the "DEC Prognostic Index." Since adrenal cortical hormones lower eosinophile levels, the sex steroids are, in respect to eosinophile levels, an anti-adrenocortical substance.

7. Patients improving on sex steroid therapy exhibit a shift in their L/N ratios which ultimately move in a direction away from the lower ratios typical of Cushing's Disease toward the high ratios as are found in Addisonian patients. Since adrenal cortical hormone produces eosinopenia and lymphocytopenia concomitantly with a neutrophilia a low ratio suggests relative adrenal cortical hyperactivity. A shift in the other direction (toward a higher ratio, under therapy) therefore suggests the operation of anti-adrenal cortical activity in the therapy insofar as it is reflected through its effects upon the leucocyte picture. Here, too, and more clearly, the greatest shift was found in patients attaining improvement. This was shown in our "L/N Prognostic Index."

This preliminary exposition of a portion of the biologic data collected in a series of correlated studies on about 200 hospitalized and non-hospitalized psychotics and psychoneurotics affords an interesting body of evidence in support of our fundamental formulations on the etiology and pathogenesis of certain psychiatric processes previously presented in the papers entitled, "The Research Background of a System of Neuroendocrinologic Formulations, Part I of Physiodynamics and Some Major Metabolic Disorders" and "A System of Physiodynamics and Its Application to the Neuroendocrinology of Psychiatry. Part II."

The implications of an association: between adrenal cortical excess and certain psychoses and of the therapeutic counterbalancing of an excess of such histamine-antidyne substances by our biochemotherapies are inherent in our data. With the availability of potent adrenal cortical stimulants and substances, some of these data and the derivative thesis as to the etiology and pathogenesis of certain psychiatric processes may in a sense be put to a test. Even though neither a positive nor a negative outcome of such a test could be considered by any means as an absolute proof or disproof of this thesis, it would nonetheless be a valued addition to the body of fundamental knowledge essential to its evaluation. Unwittingly, in many instances, and consciously, in other cases, such a test has been made. Thus, in metabolic studies of ACTH, cortisone and potent adrenal cortical extracts, severe psychiatric manifestations have occurred (even though details have not yet been published) in a number of instances as a so-called side effect. Conversely, these substances have been, to date, applied without any conspicuous success as replacement therapy by workers suspecting adrenal cortical deficiency in certain psychoses.

The next era of psychiatric advance must clarify the metabolic aspects of psychopathologic processes and in so doing, help

1. define the patterns of etiologic and pathogenetic mechanisms,
2. provide us with biologic techniques as aids in diagnosis, prognosis and therapy,
3. arm us with additional therapeutic agents.

Then and only then will our diagnoses be firmly based on precise etiologic forces and our control of the disease process related to specific pathogenetic mechanisms. Then and only then will psychiatry be graced by biochemical specifics. It is our conviction that, today, we stand on the threshold of a new era of the science of psychiatry.

## RESUMEN

Los autores estudian las diferentes facetas de una correlación entre el exceso de corteza suprarrenal y ciertas psicosis, y el modo de contrarrestar terapéuticamente un exceso de sustancias histamino-antidinas, mediante la terapia bioquimioterápica por ellos desarrollada. Al poder disponerse de potentes sustancias estimulantes córticosuprarrenales, es posible, en cierto modo, someter a una prueba algunos de estos datos, y las tesis derivadas de los mismos, en cuanto a la etiología y patogenia de ciertos procesos psiquiátricos. Aunque el resultado positivo o negativo de dicha prueba no puede considerarse como una confirmación o negación absoluta de esta tesis, es de importancia para evaluar esta tesis. Sin pretenderlo en muchos casos, y deliberadamente en otros, se ha realizado dicha prueba. Así es como en los estudios metabólicos del ACTH, cortisona, y de los potentes extractos córticosuprarrenales, en un número de casos se han presentado graves trastornos psiquiátricos, como los denominados efectos secundarios. Estas sustancias se han aplicado hasta la fecha sin ningún éxito apreciable como terapia de sustitución por los investigadores que sospechaban la existencia de una deficiencia córticosuprarrenal en ciertas psicosis.

Los adelantos psiquiátricos de la próxima era deben aclarar los aspectos metabólicos de los procesos psicopatológicos. Al hacerlo podrán ayudar a: 1) definir los cuadros generales de los mecanismos etiológicos y patogénicos; 2) suministrar técnicas biológicas como métodos de ayuda para el diagnóstico y pronóstico, y como guías para la terapia; y 3) proporcionarnos nuevos agentes terapéuticos. Solamente entonces podrán nuestros métodos diagnósticos basarse sólidamente en fuerzas etiológicas precisas y basarse nuestro dominio de las enfermedades en mecanismos patogénicos específicos. Solamente entonces podrá beneficiarse la Psiquiatría de los métodos bioquímicos específicos, siendo la convicción de los autores que hoy día nos hallamos en el umbral de una nueva era de la ciencia de la Psiquiatría.

## RESUME

Les implications d'une relation étroite entre l'excès cortical surrénal et certaines psychoses, et de l'équilibre thérapeutique d'un excès de ces substances antidyno-histaminiques par nos méthodes de biochimiothérapie, sont inhérentes à notre documentation. Vu qu'il existe maintenant des substances et des stimulants corticaux surrénaux de grande efficacité, une partie de cette documentation, ainsi que la thèse qui en découle au sujet de l'étiologie et de la pathogénie de certaines méthodes psychiatriques, peuvent en un sens être soumises à un essai de contrôle. Bien que les résultats d'un tel essai, qu'ils soient positifs ou négatifs, ne puissent en aucune façon être considérés comme une confirmation ou une réfutation absolue de cette thèse, ils n'en constitueraient pas moins une précieuse addition à l'ensemble des données fondamentales essentielles à son évaluation. Inconsciemment dans de nombreux cas, et consciemment dans d'autres cas, un tel essai a été fait. Ainsi, dans des études métaboliques d'ACTH, utilisant du

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cortisone et des extraits corticaux surrénaux de grande efficacité, on a observé des manifestations psychiatriques prononcées dans un certain nombre de cas sous forme d'effets dits accessoires (bien que des détails complets n'aient pas encore été publiés). Par contre, jusqu'à présent ces substances ont été appliquées sans succès appréciable comme thérapie de substitution par certains praticiens qui soupçonnaient une déficience corticale surrénale dans certaines psychoses.

L'ère nouvelle des progrès psychiatriques devra préciser les aspects métaboliques des processus psychopathologiques, ce qui contribuera à: (1) définir les types de mécanismes étiologiques et pathogénétiques; (2) nous fournir des techniques biologiques comme accessoires en diagnose et en prognose, et comme guides en thérapie; et (3) nous apporter des agents thérapeutiques supplémentaires.

A ce moment-là, et seulement à partir de ce moment, nos diagnostics seront basés solidement sur des forces étiologiques précises et notre technique de contrôle du processus des maladies sera étroitement apparentée aux mécanismes pathogénétiques précis. A ce moment-là, et seulement à partir de ce moment, la psychiatrie sera enrichie par les spécifiques biochimiques. Notre conviction personnelle est que nous sommes aujourd'hui au seuil d'une nouvelle ère de la science de la psychiatrie.

# Somatologic Perspectives in Psychiatric Research

## PART VI

### ENDOCRINOLOGIC ORIENTATION TO PSYCHIATRIC DISORDERS

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The somatologist, as one who deals with the biologic manifestations of the body may be called, likes to think that his field is as near the exact sciences as it is possible for the study of the phenomena of life to be.

His first contact with psychiatry is, therefore, bound to be disconcerting, to say the least. In the words of Hoskins,<sup>1</sup> "With his predilection for scientific explicitness, to the biologist, much of the psychiatric literature seems to be inept and an attempt to compensate for frustrating ignorance by semantic adroitness." The impulse is to castigate the profession for loose thinking and loose talking; for being poorly disciplined, unscientific and doctrinaire cultists.

But as he gets over his self-righteousness, he finds that by and large there is as much earnestness in psychiatry as there is in his own field, and that were he to work with the same elusive material, he could just as easily fall into the same pattern of practice and thinking. He also begins to sense some advantages—that, for instance, unlike fields in which manual skill plays a large role, psychiatrists do not as a rule fall in love with their hands and let their brains atrophy; that there is particularly among younger men a great deal of intellectual restlessness, ingenuity, and imaginativeness and a wide-awake alertness for advances in other fields which might be applicable to psychiatry. That a profession which has to its credit the creation of a revolutionary outlook on the psyche within a generation has not become more smug and arrogant, but still has enough divine discontent to look elsewhere for assistance, is to me remarkable indeed.

Nor is the tenacious clinging to the hope of discovering a somatic mechanism for mental disease a wild and illogical measure of desperation. One has only to recall the mental symptoms caused by some forms of drug intoxication, by anoxia, by certain metabolic disorders, by high fever, by disturbances of the acid-base equilibrium, to realize how well-based such hope is.

Yes, the spirit of adventure is returning to psychiatry and the intellectual courage to experiment and to hypothecate. To a field still in the early transitory stage—from the descriptive or taxonomic phase to the dynamic phase—this spirit is the essence of all epistemological progress. In some sectors of biology and medicine, the fear of being proved wrong has bred an intellectual cowardice that threatens to paralyze inquiry. An assiduous attempt has been made by some workers in these fields to avoid speculation and shun a philosophic outlook—a sure path to scientific starvation, to the lowering of science into a purely utilitarian technology. By all means, let us hypothecate and theorize and give our imagination free rein as long as: (1) in

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our thinking and writing we draw a clear line between fact and theory; (2) each link in our hypothesis is logically forged; (3) each new exploratory effort is as clear-cut and conclusive as current data and facilities permit. In this way, although our present work may be abortive or premature, it can be used as a scaffolding for the work of our successor investigators without unnecessary confusion and misdirection.

It is in keeping with this alertness that hypotheses from evolution to species-decay, from genetics through embryology to geriatrics, from strict morphology to enzymology have been involved in psychiatry.

It may be worthwhile at this juncture to say something of the principal factors thought at one time or another to be implicated in mental disease. In Bellak's<sup>2</sup> recent work on schizophrenia, there have been listed sixty-one different factors by actual count, seventeen of which were biochemical. And this number did not include Caspersson and Hyden's<sup>3</sup> findings of chromatolysis in the neurones, the role of glutathione, the Hoagland-Pincus theory of adrenal cortex unresponsivity, nor the Sackler-van Ophuijsen theory of hormonal imbalance with excessive action of the protein catabolic corticosteroids on the neurones.

While we cannot attempt even to enumerate all these factors, it may be profitable, however, by way of showing the primitive state of the knowledge of mental disease, to discuss at some length the significance of the data gathered by Hoskins<sup>1</sup> mostly from his own work, but also partly from the work of others. He has listed a number of definitive findings which he attributed to schizophrenia *per se*. Some of these were: scanty urine, with downward trend in total urinary solids and nitrogen; subnormal oxygen consumption; subnormal body temperature, blood pressure, pulse rate, blood count, and body weight. These have been attributed to thyroid deficiency, and the administration of thyroid extract has been reported to be beneficial.

Dr. Bowman<sup>4</sup> last night reported on some ingenious experiments with radioactive iodine. There were also reported other manifestations of hypometabolism, atrophy of the seminiferous tubules, poor specific dynamic action in response to food ingestion, circulatory deficiency with hypodevelopment of capillaries and reduced circulation time; poor temperature response to nitrophenol; inability to maintain a differential of ano-rectal temperature, and general metabolic unsteadiness.

In view of recent studies on the phenomenology of hypoproteinemia, by Ancel Keys et al,<sup>5</sup> and by ourselves,<sup>6</sup> it may be questioned whether the above findings are as much the stigmata of schizophrenia, *per se*, as of hypoproteinemia accompanying this mental state. This may also be applicable to the carbonic anhydrase work reported by Dr. Ashby.<sup>7</sup> I am almost tempted to predict other findings of hypoproteinemia in such cases; as, for example, blunting of the pain sense, sluggishness, and hypotonus of the viscera, a modified response to inflammatory agents, and a lowered temperature response to pyrogen.

It should now be possible to determine by quantitative metabolic studies whether these somatic findings classified by Hoskins as essential stigmata of schizophrenia were not due to concomitant protein deficiency. Such studies are fundamental and should form the base line from which psychiatric research start. For this reason, we are now formulating plans to carry them out.

In the field of morphologic studies, the work of Caspersson and Hyden on the occurrence of chromatolysis in neurones of schizophrenic patients and in rabbits subjected to stress is worth



mentioning, as well as the prevention of this chromatolysis in neurotic rabbits by the administration first of malonyl nitrile and now of succinyl nitrile. This has been apparently confirmed by the work which was reported by Dr. Papez,<sup>8</sup> in which an apparently simpler technique has been used.

Also worth-while mentioning is the attempt by Pomerat and Ewald<sup>9</sup> to determine by tissue culture differences in growth patterns between cerebral neurones in psychotic patients and those of a normal subject. It is also possible that the use of the electron microscope may uncover some subtle structural changes in the neurones of psychotics not discernible with the present microscopic technique. As far as I know, this line of inquiry has not yet been initiated.

Now for a brief discussion of the two most recent theories of mental disease. These are the Hoagland-Pincus theory<sup>10</sup> of unresponsiveness of the adrenal cortex, and the Sackler-van Ophuijsen<sup>15-22</sup> hypothesis of underbalance of the protein-catabolic effect on the neurones of the corticoids. The former may be traced to the formulation of Selye<sup>23, 24</sup> on the mechanism of body adaptation to stress. In stressful situations, there has been found in the normal subject an increase in the urinary excretion of 17-ketosteroids, accompanied by a fall in both lymphocytes and eosinophiles in the blood. These have been associated with an increase in the secretion of protein-catabolic corticosteroids, which, in turn, has been attributed to increased production of ACTH from the pituitary.

The Hoagland-Pincus group has found in schizophrenics an inadequacy of such a response in stressful situations and has drawn the preliminary conclusion that this unresponsivity of the adrenals is either causative of or implicated in the pathogenesis of schizophrenia. Such a view would imply that the use of these hormones known to cause the breakdown of cytoplasmic proteins in other tissues has a remedial effect on neurones which, as may be inferred from the psychotic symptoms, are presumably diseased. The recent reports on the precipitation of psychotic-like states by the use of either ACTH or of cortisone would seem to militate against this view.

The second hypothesis—the Sackler-van Ophuijsen formulation, as you have heard—conceives of mental disease as being the result of a hormonal imbalance, whereby the protein-catabolic action of the corticosteroids somehow becomes underbalanced and so causes a breakdown of the cytoplasmic and perhaps of the nuclear proteins of susceptible neurones, eventuating in abnormal function. It seems to check with many lines of available experimental data and to unify many otherwise independent complexes of clinical information which I hope can be brought out in the discussion. It has, moreover, the support, and, I almost say, defense of the apparently good results of experimental therapies—histamine biochemotherapy, which was its vanguard and set the formulation in motion, and of steroid sex hormone therapy, which was an outgrowth of the formulations and brought up its rear. It has, moreover, to its credit the fact that the authors were able to predict the precipitation of the development of psychotic states by the use of cortisone and of ACTH before any such effects were reported.<sup>21</sup>

The fulfillment of the prediction should, on the one hand, lend the theory great prestige, but could, on the other hand, serve as a mental trap by engendering a false sense of security. The hypothesis is an ambitious, comprehensive, sophisticated, and profound approach, and whether it is finally confirmed or refuted, it will have set in motion a great deal of timely research work—timely because of the biochemical advances now being made at such a rapid pace in endoc-



rinology, particularly in adrenocortical endocrinology. It is hardly likely that the last word on this subject has been said, and that the combination of two bodies of phenomena as complicated as those of mental disease and of the hormones with their own complex interrelationships, can be adequately covered by a formula synthesized out of the primitive data available at present. It is therefore too much to hope that these formulations will go years or even months without radical modifications.

The work reported by Dr. Papez<sup>8</sup> gives us a promising technique whereby the injury to cerebral neurones by the protein-catabolic steroids can be checked in experimental animals. If the new therapies and the formulations stand the test of future investigation and therapeutics, then a new era in psychiatry and, indeed, in somatology has been ushered in. If not, these workers have still done a great service by stimulating research work in such an important sector. It may well be that, like the alchemists of old, our ambition has outstripped our facilities by centuries, but no one can foresee at what turn of research events the truth will make its appearance.

In closing, I wish to quote Dr. Norman D. C. Lewis<sup>16</sup> who said: "We shall not forget that the historical pathway of philosophic and scientific thought is literally strewn with discarded and dead hypotheses and theories, nor should we overlook many of them which have died honorable deaths, in that they have served as stimuli for perhaps more important discoveries during their time."

We are hopeful that a better fate awaits this work than that of such mere productive martyrdom.

## RESUMEN

El primer contacto del médico, en su carácter de somatólogo (o sea el médico que estudia las manifestaciones biológicas del cuerpo humano) con la Psiquiatría, en ocasiones puede ser tedioso e incluso desesperante, pero tan pronto como el médico se desprende de sus prejuicios, halla notables compensaciones intelectuales en el campo de la Psiquiatría, en el que uno no llega a enamorarse de sus manos, y a dejar atrofiar su cerebro. El espíritu de aventura intelectual ha reaparecido en la Psiquiatría, junto con el valor intelectual para formular nuevas teorías. Por ser éste un campo que aun está en un período inicial de transición de la fase descriptiva o taxonómica a la dinámica, el citado espíritu de aventura y coraje intelectual es la esencia de todo el progreso epistemológico. Teoricemos y demos rienda suelta a nuestra imaginación, siempre y cuando que: 1) al pensar y al escribir tracemos una clara demarcación entre las teorías y los hechos; 2) cada eslabón de nuestra hipótesis esté lógicamente forjado; 3) cada nuevo esfuerzo exploratorio sea tan claro y productivo como lo permitan las circunstancias y los datos disponibles. De esta forma, aunque se considere nuestro trabajo actual como abortivo o prematuro, puede ser la estructura fundamental para el trabajo de nuestros sucesores.

Es muy prometedor el punto de vista orgánico, concebido en la teoría de Sackler-van Ophuijsen, de un desequilibrio hormonal que resultaría en una hiperacción de los córticosteroides proteínicos catabólicos sobre las neuronas cerebrales. Esta teoría cuenta además con el apoyo de las observaciones y datos obtenidos en muchos campos de la biología y de la medicina, y está reforzada por

dos nuevos agentes bioquimioterápicos aparentemente eficaces: la histamina y los esteroides sexuales, que fueron estudiados inicialmente por estos investigadores y que tienen el mérito de haber permitido a los autores predecir el desencadenamiento de los estados psicóticos en pacientes tratados con cortisona y ACTH, un año antes de que tales complicaciones fueran descubiertas clínicamente. Si estos nuevos tratamientos y teorías resisten la prueba de las investigaciones futuras, se habrá iniciado una nueva era en Psiquiatría y en Somatología. Caso contrario, estos investigadores seguirán mereciendo nuestro reconocimiento por haber estimulado el trabajo de investigación en sectores tan importantes como los citados.

## RESUME

Le premier contact du somatologiste (celui qui s'intéresse aux manifestations biologiques du corps humain) avec la psychiatrie risque d'être décevant et même ennuyeux et exaspérant, mais à mesure qu'il devient moins assuré de détenir la vérité, le domaine de la psychiatrie lui offrira beaucoup d'avantages. Ce n'est pas un domaine dont on puisse s'empêcher par un côté purement matériel en laissant son cerveau inactif. L'esprit d'aventure et le courage intellectuel d'émettre des hypothèses et des théories revivent. Dans un domaine qui est encore au début d'un stade de transition—entre la phase descriptive ou taxonomique et la phase dynamique—cet esprit est l'essence de tout progrès épistémologique. Il faut absolument faire des hypothèses, émettre des théories et lâcher les rênes à l'imagination dans la mesure où: 1) Dans notre pensée et dans nos écrits nous traçons une ligne de démarcation nette entre le fait et la théorie; 2) Chaque nouvelle étape de l'hypothèse est logiquement établie; 3) Chaque nouvel effort explorateur est aussi défini et fructueux que le permettent les facilités et les données actuelles. De cette manière, quoique notre présent travail puisse se montrer abortif ou prématuré, il peut servir d'échafaudage pour les travaux des investigateurs qui nous succéderont.

Le fondement organique sur lequel est basée la théorie Sackler-van Ophuijsen du déséquilibre hormonal, ayant pour résultat une action excessive des protéines corticostéroïdes cataboliques sur les neurones cérébraux est pleine de promesses.

Cette théorie est appuyée indirectement par des observations et des données provenant de nombreux domaines de la biologie et de la médecine; elle est corroborée par deux nouvelles biochimiothérapies—l'histamine et les stéroïdes sexuels—toutes deux instaurées par ces auteurs et elle a en sa faveur d'avoir permis à ces auteurs de prédire, un an avant que ces complications n'aient été constatées cliniquement, l'occurrence d'épisodes psychotiques chez des malades traités par la cortisone et l'ACTH. Si ces nouvelles thérapeutiques et théories supportent l'épreuve d'investigations futures, une nouvelle ère aura été ouverte en psychiatrie comme en somatologie. Dans le cas contraire, ces auteurs devront néanmoins être félicités pour leurs recherches pleines d'intérêt dans cet important domaine.

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# ENDOCRINOLOGIC ORIENTATION TO PSYCHIATRIC DISORDERS

## DISCUSSION\*

*Edwin Gildea, M.D., Moderator*

MODERATOR, DR. E. GILDEA (St. Louis): The meeting is now open for discussion. To start things off, I will call on Dr. Karl Bowman, who, I see, has made many notes, and I am sure he is prepared to discuss this subject.

DR. K. BOWMAN (California): Ladies and gentlemen, I have been very much interested in what has been presented tonight, because it is completely in line with my own thinking.

Back in 1920, I first started working with basal metabolism and biochemical studies in schizophrenia. The only trouble was, we had so few tests in those days. When you wanted to try endocrine substance, you did not have much of anything except some adrenalin, and one was really stymied until biochemists, endocrinologists and others developed a greater knowledge so that the psychiatrist could apply it.

Now there were two or three points which were brought up that I would like to speak about specifically. One is the concept that electric shock works by liberating histamine. I think it is important to keep this in mind. If you give a patient electric shock therapy and only produce unconsciousness, irrespective of the amount of electricity, you do not help your patient. Usually, the patient is just knocked unconscious by the large electrical current and is made worse, more tense, more anxious, and the effect is harmful. However, so far as I know, there is no clear evidence to show that the production of the convulsion affects the liberating of histamine.

In reference to the comment made on the release of histamine by insulin, we have had in our experience one case of a perforating gastric ulcer following insulin treatment. This patient had a history of having had a gastric ulcer in the past. Our Professor of Surgery was a little critical, in that we gave insulin treatment to the patient with that previous history, because, he said, the insulin increases the secretion of hydrochloric acid, therefore increasing the danger of perforation.

Now, the idea of an endocrine base for dementia praecox has been with us, as the papers reported, ever since Kraepelin formulated the idea. He himself said it might be a metabolic disorder due to the disease of the thyroid and gonads. That is still something for us to keep in mind. Mott, in about 1915-18, presented his idea of testicular atrophy and cerebral oxygen deprivation. It is interesting that Mott, who was certainly an organicist, was also led by some of the psychoanalytic theories, particularly the Adlerian. Mott went on to explain that the individual with testicular atrophy had a great feeling of inferiority, and that this conflict caused his schizophrenia. Starting out as good physiology, it ended in psychoanalytical psychology.

The theory that has been spoken of tonight suggests the breakdown of the cells of the nervous system as a result of several causes. I will say that we have been doing lobotomies for nearly a year now, and when the lobotomies are done, a section of the brain is taken out. We then give the patient radioactive iridium. This work will be reported in the future. Dr. Nathan Malamud who has been examining these sections of brain from old chronic schizophrenics, many of whom have had insulin and electric shock, so far has not found any evidence whatsoever of abnormality in these brains. He cannot duplicate any of the reported changes that some investigators claim to find in schizophrenia. It may be those are occurring in some other sections of the brain and not the section of the lobotomy.

I think we have a great tendency in psychiatry to think that the person can have only one disease, and then that there can be only one cause for this disease. And so we approach all our patients with the thought that the patient has disease X, and nothing else is the matter with him, and disease X is due to one single cause — Y, which we are still looking for. It seems possible that our patient can have a combination of psychiatric diseases just as much as they can have a combination of physical diseases. And yet we cannot seem to come to that way of thinking.

Like Adolph Meyer, I am a pluralist and doubt if the etiology of schizophrenia or a manic-depressive state will be found related to a single cause. It is barely possible that it will be something like this: that there are ten factors, and the presence of any five will produce the disorder. Now, if you assume a possibility like that, you can realize the complication and difficulties you are going to have in trying to figure out the cause of the disease. That was not my thought originally. That was the thought of Professor E. B. Wilson, who was the Professor of Vital Statistics at Harvard . . . I wonder if we are not too obsessed with the idea that there is a single cause for schizophrenia and that we are concentrating to find that single cause.

Thank you.

\*Due to limitations of space the discussion has been edited and is presented in abridged form.

EDWIN GILDEA, MODERATOR

MODERATOR GILDEA: Does anyone else wish to make some comments?

DR. M. RINKEL (Boston): Following Dr. Bowman's discussion and the comments about the Boston Psychopathic Hospital, I feel I have to make a few remarks.

I was greatly impressed with the work of the Creedmoor Group on schizophrenia and its relationship to histamine, and followed the presentation with great respect and attention. A wealth of knowledge and important data were reported to us tonight, and the authors deserve to be congratulated on their excellent work. In the endeavor to investigate the problem of schizophrenia, at the Boston Psychopathic Hospital, we have approached the problem from a different angle. In order to understand a disease, or a psychosis, it would be of great advantage if one could experimentally produce a psychosis. We are in the fortunate position to have a chemical, a derivative of ergot, with which we could produce a transitory psychotic disturbance. Histamine is found in ergot, and this new chemical, an ergot derivative, is called d-Lysergic acid diethylamide tartrate. It is a very remarkable chemical. We have given it to a number of volunteers, psychiatrists, nurses, students, and occupational therapists in an amount as small as one gamma per kilogram body weight, and we observed mental symptoms which one could say were the negative of what we have heard today as a result of the treatment with histamine. While with histamine treatment the patient thought more clearly, our patients had difficulty in thinking. They were blocked; they wanted to say things, but they could not express themselves. They had strange sensations; their limbs felt like lead. They felt they could not get up or they could not walk. However, on command, they walked quite freely. They had illusionary experiences. They saw figures on the wall, and the walls were moving. Some became quite silly, laughing without being happy or gay, and some became very talkative. However, the content of what they produced was very shallow. We have recordings of it, and it is almost gruesome to listen to that, and at some future meeting we will present it. We are preparing it now for publication. The symptoms are temporary; they last for several hours, and in the late afternoon they disappear. Paranoid symptoms come up and hostility develops against the observers and against everybody. One girl was extremely disturbed and felt somewhat depressed on the following day, but none were impaired for work, at least on the following day.

DR. CO TUI (New York): Is it a form of drug intoxication — a type like that of cocaine poisoning?

DR. RINKEL: I think it is different from cocaine poisoning, and it is different from d-desoxy-ephedrine psychosis. There are also definite differences with regard to mescaline. Bromide poisoning shows many different symptoms. No other chemical or drug is known to me that would bring about such definite mental changes, with only traces of a chemical given by mouth, as is the case with L.S.D.

DR. BROWN: What is the duration of the psychosis produced, and what is the nature of the memory of the experience after it is over?

DR. RINKEL: The psychotic disturbance lasts about 24 hours. The patient will remember everything. In fact, every individual afterward wrote a report of his own experiences.

DR. R. SACKLER: Were there any physical manifestations?

DR. RINKEL: Yes, there are some physical manifestations. There was lowered blood pressure in some instances. Some had clammy hands, perspiration and dry mouth; not much more, at least as we have observed. There were a number of subjective symptoms, which objectively could not be corroborated.

DR. ACKERLY: Did you give histamine?

DR. RINKEL: Not yet. Many of the observations I have mentioned today will be again presented after conclusion of our experiments.

MODERATOR GILDEA: Are there any other questions?

DR. M. SOLOMON (Chicago): May I say a few words on the so-called mind-body problem in connection with the viewpoint under discussion.

The human organism or body is a psychophysiological machine. Although it is basically a physiological or physicochemical machine, its activities, for the purpose of this discussion, can be classified into two main groups. One type of functioning is called mental or psychological and includes thinking, feeling, wishing, imagining, reasoning, etc. Such mental activity is as much bodily as it is physiological activity. The other type of activity is called bodily physiological (which is basically physicochemical) and includes skeletal and visceral functioning. All these activities — both the various so-called psychological and the various physiological and physicochemical activities — are bodily. There is no special entity like the mind or psyche divorced from the living organism or body. These mental activities are part and parcel of the living human body or organism which is psychophysiological. Whereas the Christian Scientist says it is all mind and no body, the truth is that it is all body and no mind (in the sense of a special entity). The term "the mind" has been used as a generic term which has trapped us, since we have been in the habit of differentiating it from the body instead of including under the term, "the body," all mental as well as physiological processes. Instead of battling with the problem of

the relation of the so-called mind to the so-called body, we should speak of the relation of the psychological or mental to the physiological and vice versa, both of them, however, being bodily or organismal. The psychological and physiological (skeletal, visceral and hormonal) levels are interrelated and may influence each other. Basically it is all physicochemical. Mental functioning is just as much bodily as skeletal, visceral or endocrinal. They are all interrelated and integrated into a total, unified bodily machine.

This approach, I think, helps toward clarification of these problems, accepts the non-existence of a separate mind or psyche, regards mental activities as bodily, and reduces the issue not to the relations between a mind (a term generically used for so-called mental activity) and a body (currently loosely used for physiological as distinguished from psychological activity) but to the relations between psychological and physiological, both taking place in the body or organism and thus really being bodily.

Scientifically, then, there is no mind-body problem but a psychological-physiological problem within the total body or organism.

MODERATOR GILDEA: Thank you. Are there any further comments or questions?

DR. GOODMAN: An allusion was made by Dr. Sackler as to the possibility that the favorable effects of histamine were related to improved cerebral circulation. I wonder if measurements of the oxygen uptake of the brain, according to the methods of Kety and Schmidt, were made prior to the use of histamine in these patients or in any group, and during the test and afterward, in order to determine whether it was actually an improvement in the cerebral circulation according to the only purely objective method we have of determining that particular situation.

DR. WILSON: I would like to ask how many psychoneurotics or psychotics are treated, and just what their feelings are and their results, so far as, shall we say, the cure goes.

DR. W. ASHBY (Washington): I would like to know how the sex hormones fit into this picture. I have in mind the work showing an inhibitory effect of diethylstilbestrol upon succin oxidase and the recent work of Wright and Burk showing the reversal of this effect by progesterone and testosterone.

MODERATOR GILDEA: There is one thing I would like to emphasize, and that is that the Creedmoor Group has brought out the fact that there really is not any evidence of adrenal deficiency in schizophrenic patients. At St. Louis, we have been having difficulty in demonstrating that schizophrenics were responding poorly to various stress tests that should show adrenocortical dysfunction or partial dysfunction. With some 25 very ill schizophrenics of a long term, we have only found one schizophrenic that was a little sluggish in response to stress tests like heat and injection of adrenalin and so forth; whereas, in the Hoagland-Pincus series there were about 70 per cent that failed to respond adequately.

I think we should give the Drs. Sackler a chance to close. We appreciate being overwhelmed by so much experimental data.

DR. RAYMOND SACKLER: In response to the question as to oxygen uptake according to the methods of Kety and Schmidt, may I state that we have not carried out this procedure. However, others have reported an increased cerebral flow . . . It is interesting to interject that we have noted a fairly marked reduction in the confusion and memory defect following ECT in patients either pre-treated with histamine or receiving histamine concurrent with ECT.

DR. M. SACKLER: Among the patients we have treated there have been many more schizophrenics than psychoneurotics. Our experience with the latter group, therefore, is relatively limited but does point in a certain direction. Among those psychoneurotics we have treated, we have found histamine to be extremely helpful in the alleviation of acute anxiety and/or reactive depression. We have, also, noted that histamine therapy reduces blocking and improves productivity qualitatively as well as quantitatively.

We cannot answer Dr. Ashby's question in relation to succin oxidase because we have not done any work with this enzyme. However, as reported, the sex hormones do fit into the picture as a therapeutic weapon. We have proposed that relative deficiencies of these hormones may be involved in the etiology and pathogenesis of the disease. The antidyne effects of progesterone and testosterone as against diethylstilbestrol in relation to succin oxidase are interesting.

DR. A. SACKLER: As to adrenocortical deficiency, Dr. Gildea raised an interesting question, and I would like to take that up first. Sometimes we get involved in intricate test procedures and overlook the obvious. Consider, for example, the fact that bio-assays of adrenocortical hormone are the work-performance test of Ingle and Nezamis. Now, if you want a good work-performance test, try wrestling with a disturbed schizophrenic as we have had the misfortune to do. I have seen 95-pound catatonics throwing 150- to 200-pound men around. This could not be viewed as evidence of poor "work performance."

A few words on the subject of adrenocortical reserve. If we drive a car at the rate of 90 miles an hour, then we test its reserve and if the car goes 100 miles an hour, it has a reserve of ten miles an hour. On the other



hand, when driven at 10 miles an hour, the same car has a reserve of 90 miles an hour. We think it is very dangerous to confuse reserve with total potential output.

In relation to Dr. Solomon's remarks, may we say that we agree. We do not believe that there is any split between the psyche and the soma. Thinking is as much a physiological function as walking.

We found Dr. Bowman's comments very interesting. However, there is one we would like to elaborate upon. We stated that it was only early in our work that we thought ECT produced its effect primarily by a liberation of histamine. In our papers, we pointed out that the electric shock therapy could effect both pituitary and neuronal function and also indicated that there could be other humoral or glandular mechanisms.

While we have demonstrated an increased gastric hydrochloric acid, we reported that it could be due to histamine stimulation, or vagal stimulation, or yet still have nothing to do with histamine whatsoever.

As we reported tonight, Kraepelin, in one of his last lectures, made the remark that he thought dementia praecox may be related to the suprarenal gland. This was in his closing lecture of a series delivered over fifty years ago.

As to whether a number of factors may be responsible for schizophrenia, we, too, do not believe there is just one. Hormonal imbalances or dysequilibria, as etiologic and pathogenetic factors, seem to be operative in different combinations. We believe that these dysequilibria vary with histamine, insulin, thyroid, gonadal and adrenal hormones participating in different ratios in different individuals. That is what we have been trying to piece together in the experimental work we have reported. We do not believe it need necessarily be an absolute deficiency of one of these hormones, but, rather, it may be what we refer to as an operative deficiency. We have gone into this in one of our papers, and we found that it was dangerous and confusing to indulge in static thinking about any one gland. Each gland had to be thought of dynamically in its multiple and changing relationships to many other glands. We have, therefore, differentiated between the "absolute output" of the gland, its "relative output" and the "operative concentration" of its hormone in relation to the different end-organs. These are all different parameters. Failure to appreciate this may lead to a great deal of confusion.

Different workers including our group have defined different individual elements of schizophrenia. Many of these findings have, in the past, been erroneously viewed as unrelated, even conflicting and mutually contradictory. We have drawn an analogy to the blind men and the elephant. Perhaps, you have heard that story, where one man holds onto the elephant's tail and says the elephant is a rope with a tassel; and the next man feels the leg, and says it is a tree trunk. The third man says, "No, it is a tusk which is smooth and comes to a point." The fourth man says, "It is a flexible tube." Such a circumscribed approach has been as confounding as schizophrenia is complex. It is our opinion that many of the seemingly diverse elements do fit together in an integrated picture and that they constitute various aspects of a definitive pattern. We have found common denominators of different therapies which also seem to point to an integrated neuroendocrine basis for schizophrenia.

What has been lacking, in the past, is perspective upon the disease. What is needed is an unifying concept which integrates all findings.

# Electromyographic Studies of Muscular Tension in Psychiatric Patients Under Stress

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There is considerable evidence that increased tension of the skeletal muscles constitutes one of the important physiological manifestations of emotion.<sup>7</sup> This being so, the study of muscular tension in the psychiatric disorders should provide important data concerning the physiology of the pathological emotional states associated with these disorders. However, very little experimental work has been carried out in this field. The available information is meager and may be summarized by the statement that most investigators find evidence of greater than normal muscular tension in psychiatric patients. This conclusion, which has been reached both by clinical observation<sup>1</sup> and by the use of recording techniques, such as electromyography,<sup>7, 9</sup> is important in itself, but it requires much further supplementation.

The following questions are among those which require an answer: (1) Is the level of muscular tension greater than normal in all types of psychiatric patients? (2) Is muscular tension nearly always abnormally elevated in psychiatric conditions or does the psychiatric patient show greater tension only in response to emotionally upsetting stimuli or stress? (3) Under conditions of stress, what is the temporal course of tensional response in psychiatric patients? Does it differ from the normal and if so, in what respect? (4) Is there individual constancy of muscular tension under stress, i.e., will the individual with high tension in one stress situation also tend to show high tension in another situation? The main purpose of the present investigation was to provide data bearing on these questions.

The method of studying muscular tension employed in this investigation was to record quantified electromyograms (EMG's) while subjects were undergoing three stress tests of varying type. The EMG was used because it affords probably the most accurate and sensitive method of measuring muscular activity. The present procedure is an extension of that employed by Malmo and Shagass<sup>9</sup> who recorded EMG's together with other physiological measures in the Pain-Stress Test, which is one of the tests employed in the present study. Malmo and Shagass found that measures of skeletal-motor function differentiated particularly well between psychiatric patients and controls. It was considered, however, that information bearing on the questions raised above could only be obtained if an accurate method of quantifying the EMG were available and if several stress procedures of varying type were employed. These methodological requirements are fulfilled in the present study, the first by the development of an electronic integrating device<sup>2</sup> which is employed here for the first time, and the second by the provision of two additional stress tests.

In addition to the purposes stated above, the present study was designed to deal with two further questions raised by the results of Malmo and Shagass:<sup>9</sup> (1) They took a record of finger

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movement similar to the Luria tremorgram, and scored it so as to provide a quantitative measure of total irregularity in finger movement. This measure yielded significant differences between patients and controls.

Since the measure of finger movement irregularity reflected one aspect of muscular activity it became a matter of considerable interest to determine whether this aspect was a function of the level of tension in the associated muscles. Simultaneous recording of finger movement and muscle potentials from the arm in the present study was designed to provide the data required for this correlation. (2) Malmo and Shagass found that physiological reactivity in early schizophrenia was very high, being similar to that found in anxiety states. This raised the question of how reactivity to stress in chronic schizophrenics compared with that found in early cases. To provide data on this point a group of chronic schizophrenics was included in the present investigation.

## METHODS

### *Experimental Population*

The original subject population employed in the stress experiments was composed of 76 psychiatric patients and 21 normal controls. Due to various technical difficulties, all of the quantitative tension data for one patient were lost, reducing the patient group to 75. Also, certain portions of the data were not obtainable for a small number of subjects. The numbers of cases for whom data were available for each stress test are shown in Table I. The description of the subject groups will include the 75 patients for whom tension data on at least one stress test were available.

TABLE I  
*Final Subject Population*

Test	Electrode Placement	Number of Cases in each Subject Group			
		Controls	Psychoneurotics	Acute Psychotics	Chronic Schiz.
Pain	neck	20	42	14	16
Pain	arm	20	42	13	16
Discrim.	arm	21	44	14	10
Mir. I	arm	19	43	12	16
Mir. II	arm	20	43	13	13

1. *Patients:* Of the patients, 17 were chronic schizophrenics who had been committed to a general hospital. The remaining 58 were unselected patients from the psychiatric wards of a general hospital, which does not accept patients on a commitment basis.

For analysis of data, the patient population was divided into three groups: (a) psychoneurotics, (b) acute psychotics, (c) chronic schizophrenics.

(a) *Psychoneurotics:* There were 44 patients in this group, 20 male and 24 female. The mean age was 37.6 years, ranging from 17 to 60. In 39 cases, pathological anxiety or tension was considered to be a prominent clinical manifestation. In 24 of these 39 cases the following clinical features were of importance, in addition to anxiety:—psychoneurotic depression (15 cases); tendency to alcoholism (4 cases); hysterical personality, migraine headaches, depersonalization syndrome, Raynaud-like syndrome, drug addiction (one case each). Of the 5 cases in whom anxiety and tension were not considered to be prominent, one was a case of anorexia nervosa and in the remainder alcoholism was considered to be symptomatic of personality disorder.

(b) *Acute Psychotics*: The 14 patients in this group ranged in age from 19 to 61; mean age was 33.4 years. There were 6 males and 8 females. Eleven cases manifested symptoms of a schizophrenic nature, one was an agitated depression, while the remaining two presented paranoid reactions, with one of the two complicated by possible organic brain damage. All cases in this group showed acute (not chronic) psychotic symptoms, and none had ever been committed to a mental hospital.

(c) *Chronic Schizophrenics*: All 17 patients in this group were males. Age range was 19 to 37; mean age was 28.5. Duration of illness ranged from 2 to 9 years, with a mean duration of 4.5 years. Period of hospitalization varied from 1.5 to 6 years, averaging 3 years. A clear remission since onset of illness had occurred in only one patient, who, however, had required continuous commitment for one year before participating in the present experiments. All cases manifested either delusions, hallucinations or both. Classification as to type of schizophrenia was:—paranoid, 10 cases; simple, 4; catatonic, 2; undetermined, 1. This group was clearly distinguished from the acute psychotic group, insofar as all of the patients manifested evidence of personality deterioration, and all had been committed.

2. *Normal Controls*: This group contained 7 males and 14 females. Mean age was 26.0 years, with the range from 18 to 39. There were only 2 subjects familiar with mental hospital procedures and none familiar with the procedures employed in the present experiments.

#### *Stress Procedures*

Electromyograms were recorded as part of a battery of physiological measurements taken simultaneously under three standard conditions of stress. In the order presented, the three stress tests were: (1) Pain-Stress, (2) Rapid Discrimination, (3) Mirror Drawing. Prior to entering the experimental room, the subject was taken to a separate room. Here he was reassured and instructed about the first test. His forehead was then blackened, electrodes were placed, and his blood pressure was taken. Finally, the subject was taken to the experimental room where he was seated in the experimental chair and asked to relax as much as possible. Following a rest period of 9½ minutes the subject was asked to place his head in the optical frame which served to keep the head steady for pain stimulation.

*Pain-Stress Test*: The procedure employed in this test has been described in detail in a previous report.<sup>9</sup> Briefly, the test involved a series of 12 pain stimuli presented in a fixed order of intensity by a Hardy-Wolff thermal stimulator. Stimuli were 90 seconds apart, with a duration of three seconds, except for the twelfth, which lasted only one second. The order of intensities in watts was 500, 270, 340, 400, 270, 340, 400, 270, 340, 400, 500, 500.

During the test the subject sat leaning forward slightly with his chin in a rest, and both arms resting on the arms of the chair. Care was taken to insure the maintenance of both forearms in a standard pronated position. The subject's right forefinger rested on a button which he was instructed to press during stimulation when he thought that the heat on his forehead was about to become painful. The subject's eyes remained closed throughout the test.

The subject was requested not to talk during the test, except when the examiner asked him a question. Exactly 30 seconds following each stimulus the examiner asked the subject two questions:—"How did that feel to you?" and "Did you press the button?"

*Rapid Discrimination Stress Test*: The materials for this test consisted of 20 sets of circles. Each set contained 6 numbered circles of varying size. The sizes were sufficiently similar to make discrimination somewhat difficult. The 20 sets were photographed on slide-film, for projection on a screen. As projected, the circles were white against a black background. The subject was required to judge which of the 6 circles was the largest and to respond to each set by stating the number of the largest while simultaneously pressing a button with his right fore-

finger. If his judgment was incorrect, or if he did not respond before the next stimulus (set of circles) was shown, the examiner sounded a buzzer. The same series of 20 stimuli was repeated 3 times. Interval between stimuli was 5 seconds the first time the series was presented, 3 seconds the second time and 2 seconds the third time. A 30-second period intervened between each presentation of the series. Recording was started 40 seconds before the beginning of the first presentation and continued for 70 seconds after the end of the third repetition of the series.

*Mirror Drawing Stress Test:* This test involved two mirror drawing tasks. The first, which has been described by Wechsler and Hartogs<sup>18</sup> required that a straight line be drawn between two numbered points,  $5\frac{3}{4}$  inches apart. The material for the second test consisted of a printed circle,  $2\frac{1}{2}$  inches in diameter. On the side nearest the subject there were two dots, one inside, the other outside the circle at a distance from it of  $\frac{1}{8}$  inch. These dots were the starting points for two circles which the subject was required to draw in succession.

Each mirror drawing test was divided into three periods: (1) a "rest" period of 30 seconds, (2) an instruction period of 50 seconds during which the subject took pencil in hand, placed the pencil on the starting point, and listened to the instructions, (3) the performance period. The time limit for each performance was 3 minutes, but few subjects required more than 2 minutes. It should be stated that all subjects except normal controls and chronic schizophrenics had received the first mirror drawing test (straight line) during routine clinical psychological testing before the experiment. However, the second (circle) test was new to all subjects. The first test was retained to permit closer equalization of the mirror drawing experience of all subjects. Practice favored the psychoneurotics and acute psychotics over the controls. From the standpoint of practice on Test 1, controls and chronic schizophrenics were directly comparable.

#### Apparatus

*Electromyograms:* EMC's were recorded with an Offner Type C electroencephalograph. For neck EMC's chlorided silver leads, of EEG type, applied with collodion, were employed. One was placed over the fifth cervical spine, the other on the left side of the neck, 1 inch superior and 2 inches lateral to the first. Arm EMC's were recorded from the flexor surface of the right forearm. Leads were 1 inch squares, obtained by cutting down regular Cambridge EKG leads, and were held in place by rubber straps. The lower lead was placed at the wrist, while the upper was centered halfway between the styloid process of the ulna and the medial epicondyle of the humerus and at the junction of medial and outer two-thirds of the forearm. A grounded electrode was attached to the right arm to help eliminate interference.

*Muscle Potential Integrator:* Since muscle action potentials, as recorded with EEG equipment, have a modal frequency varying between 40 and 50 cycles per second, accurate quantification of the EMC constitutes a formidable problem. To overcome this problem, an integrating device was designed and built by one of us (J.F.D.). It has been described in detail elsewhere.<sup>2</sup> This integrator measures the energy spectrum included in a band with the lower frequency limit at 25 cycles per second and the upper at 5000. It is driven by the EMC, but does not interfere with the recording of the EMC. It provides meter readings which are proportional to the area under the curve of the EMC. The periods of integration may be set for the desired time interval. These features provided quantitative measurements which were proportional to the mean amplitude or voltage of the EMC for the period of integration.

*Integrator Timing:* The integrator was arranged so that it could be started either by a manual control or by a relay activated by the timing circuit used to control pain stimulation. The dial

needle remained stationary at the end of an automatically timed period of integration. Discharge to zero was accomplished by means of a manual control. In all experiments a minimum of 10 seconds was allowed between integrations, so that the operator could note the readings and discharge the condensers.

Two integrators were employed in this study. Neck and arm EMG's were integrated during the Pain-Stress Test. Only arm EMG's from the flexor surface were integrated during the other stress tests.

For the Pain-Stress Test, four 10-second integrator readings were taken over the period of each stimulus. The stimulus relay automatically started the integrator at the beginning of pain stimulation. Considering the onset of stimulus as zero time, the integrations were taken at 0 to 10, 20 to 30, 40 to 50 and 70 to 80 seconds. Thus 40 of the 90 seconds of EMG taken in the interval between two stimuli were integrated. For the Rapid Discrimination and Mirror Drawing Tests, 30-second integration periods were employed. For Rapid Discrimination, the first integration was started 40 seconds before the first series. Considering the start of this integration as zero seconds, the succeeding periods of integration started at 40, 80, 120, 170, 210, 260, 300 and 340 seconds respectively. For the Mirror Drawing Tests a single 30-second integration was taken during the "rest" period, another was taken during the instruction period and successive 30-second integrations were taken during the performance period until the test was finished. Integration was stopped as soon as the subject completed the test.

#### *Treatment of Data*

*Calibrations:* When the stress experiments were carried out, oscillator equipment was not available for routine calibration. For routine purposes, DC signals were employed. However, standard calibration curves relating integrator readings to 50 cycles per second oscillator input at all amplifications were obtained. Since the use of DC calibrations provided no method of converting the integrator readings directly to microvolts of AC input, it was necessary to employ an amplification standard to which all integrator readings could be converted. This standard was selected as 10 microvolts per mm. of pen deflection on the EEG at the most commonly used EEG gain setting. From the DC calibrations the actual microvolts per mm. at this gain setting for a particular record were determined. This provided the factor needed to convert the readings to 10 microvolts per mm. for the most frequently used gain. The AC calibration curves permitted determination of the factors required to convert integrator readings taken at all other gains into integrator readings at this standard gain. By use of these factors all integrator readings could be converted into a common unit, directly proportional to microvolts. For convenient reference, this "integrator" unit will subsequently be designated as the "I-unit." The "I-unit" conversions represent the meter reading that would have been obtained if the recordings had been taken under uniform conditions of amplification. All values for the Pain-Stress Test were converted to "I-units" for 10 seconds; for the other tests all values were converted to "I-units" for 30 seconds.

*EKG Correction:* Since EKG's were almost invariably recorded in the neck EMG it was necessary to correct for any artificial increase in the integrator readings produced by the QRS complex. This was done approximately by determining from the AC calibration curves what



integrator reading would be expected for a signal of the amplitude and frequency of the R-waves in a particular EKG and deducting this expected reading from the obtained neck EMG reading.

*Statistics:* The conventional criterion of statistical significance, 20 to 1 odds against chance, was employed in interpreting the reliability of observed differences and relationships.

*Age and Sex:* The numerical muscular tension values for the sexes were compared and were also correlated with age in order to determine whether age and sex exerted any influence. No statistically reliable sex differences or correlations with age were found, indicating that there was no need to correct for these factors in assessing the data.

#### *Validation of Muscle Potential Measurement as a Sensitive Tension Indicator*

It has been shown that muscle action potentials increase in amplitude as the muscle is required to do more work.<sup>3, 17</sup> These studies indicate that the EMG amplitude may be taken as an accurate and sensitive indicator of muscular tension. Since the results of the present study were interpreted upon this assumption, it was felt that a check upon the relationship between EMG amplitude, as measured by our equipment, and some clearly defined standard of muscular tension was indicated. For this purpose we measured the action potentials in the preferred forearm during a graded series of dynamometer pulls.

There were 20 subjects, 11 normal controls and 9 psychiatric patients. Nine subjects were female. The subject gripped a Smedley hand dynamometer with the preferred hand, held in a standard position. The examiner instructed the subject to pull the dynamometer to the required kilogram value and to maintain the grip until told to release it. A practice series was carried out beforehand. In the experimental series the order of pulls in 1 Kg. steps was 1 to 10, 10 to 1, 11 to 20, 20 to 11 Kg. for men and 1 to 10, 10 to 1, 11 to 16, 16 to 11 Kg. for women. The actual pull was noted. Duration of pull was 9 seconds. Continuous EMG's from the flexor surface of the forearm were taken with a Type D Offner EEG from lead placements like those used in the stress experiments. The action potentials for the 4-second interval from 3 to 7 seconds after the start of pull were measured by means of the integrator. At the end of the recorded pulls, the subject was asked to exert his maximum pull upon the dynamometer for 3 trials, in order to provide an indication of physical strength.

The integrator data were converted to microvolt equivalents of a 50 cycle sine wave signal generated by an audio-oscillator and calibrated with a microvolter. Fig. 1 shows the curves obtained by relating mean microvolts to degree of physical tension in the male and female groups. It is apparent that a lawful relationship was present and that amplitude of potential increased with increased physical tension. The curve for female subjects was above that of the males, indicating that, on the average, the same degree of muscular work was accompanied by more electrical activity in the females. It seemed that this difference in EMG amplitude might be due to the difference in muscular strength between the sexes, since the maximum dynamometer pulls of the female group were all lower than those of the males. To explore this possibility the correlation between mean voltage per kilogram pull and maximum pull was determined. The rank order coefficient was  $-0.61$ , indicating that the greater the muscular strength, the less the electrical potential produced by the muscle for a specified dynamometer pull. The

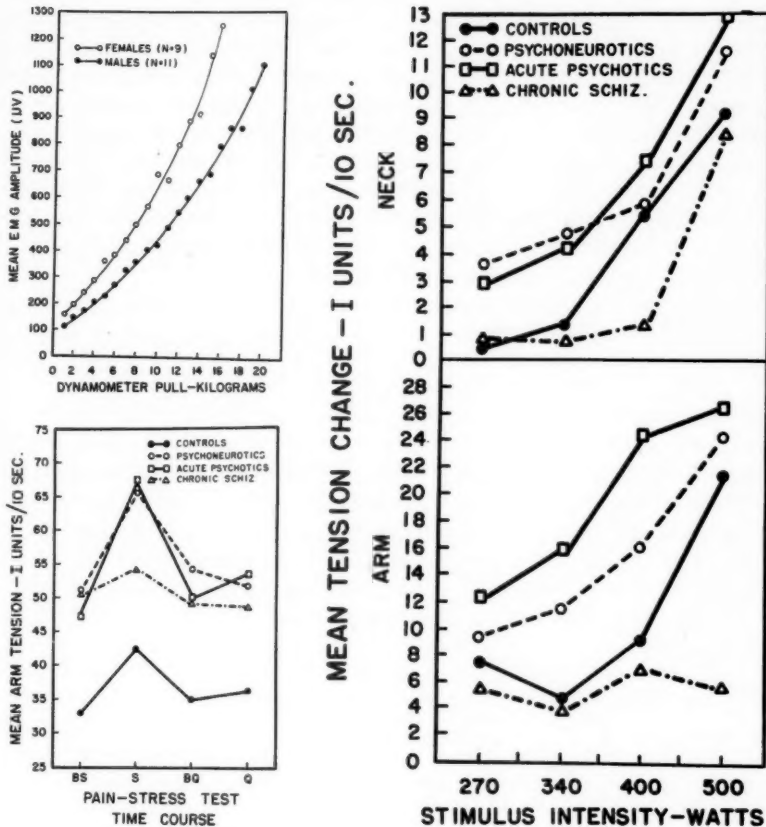


FIG. 1. Top, left: Integrator readings in microvolts as a function of dynamometer pull in kilograms.

FIG. 2. Bottom, left: Mean arm tension during different phases of the Pain-Stress Test in the four subject groups. BS, before stimulus; S, during stimulus; BQ, before questions; Q, during questions.

FIG. 3. Right: Mean change in arm and neck tension plotted against intensity of thermal stimulation. Only stimuli of 3 seconds' duration are plotted; stimulus 12 (500 watts for 1 second) is omitted.

sex difference in EMG may then be attributed mainly to a sex difference in muscular strength. It should be noted that the sex difference was smallest with the lowest pulls, which probably accounts for our failure to find sex differences in the tension data from the stress studies.

The average curves in Fig. 1 are curvilinear, but individual subjects varied considerably with regard to the linearity of their curves; some were almost perfectly linear up to 20 Kg., others were curvilinear throughout. On the average, however, the lower part of each curve, up to 6 or 8 Kg. pull, tended to be linear, with the upward acceleration of the curve increasing as the

amount of pull increased. The general linearity of the curves at the points represented by lower degrees of muscular pull is of some importance, since most of the potentials in the stress studies were at an amplitude level well below that found with 1 Kg. pull. Consequently the relationship of the potentials, taken under stress, to physical tension was probably nearly linear.

A spring scale calibrated in units of 200 grams was used to provide additional data for the range between 0 and 2000 grams. Four subjects, two men and two women, were tested in this range, using a method similar to the one employed with the hand dynamometer. In this experiment the steps were 200 grams. The inference from the dynamometer data was proven correct; linear curves were obtained in this range from 0 to 2000 grams. It should be noted further that in this lower range no consistent sex difference was observed.

The results of this dynamometer study show that integrated muscle action potentials, as measured in this study, provide an accurate indicator of muscular tension, thus establishing the validity of the measure.

## RESULTS

### I. Pain-Stress Test

#### 1. Levels of Muscular Tension

The mean muscular tension recorded during the entire Pain-Stress Test is shown for each group in Table II. The only statistically reliable difference in tension level between the various groups was that between the mean arm tensions of the control and psychoneurotic groups. However, it should be pointed out that the mean arm tensions of the three patient groups were approximately equal and that, if the two psychotic groups are considered together and compared with the controls, their mean arm tension was reliably higher. No reliable differences in mean neck tension were found.

TABLE II  
Mean Muscular Tension During Pain-Stress Test  
Tension Levels in 1-Units per 10 sec. Integration

Subject Group	Arm		Neck	
	Mean	S.D.	Mean	S.D.
Controls	35.7 ✓	20.6	34.3	15.5
Psychoneurotics	53.5	32.9	35.0	14.8
Acute Psychotics	58.3 ✓	43.6	39.2 ✓	20.9
Chronic Schiz.	51.2	30.3	33.0	17.1

If muscular tension were generally higher in psychiatric patients, regardless of the external conditions, one would expect neck tension as well as arm tension to be greater in patients than in controls. Since only arm tension was reliably higher in the patients, the data suggest that the higher arm tension of the patients represented greater tensional response to some feature of the stress situation, apart from immediate pain stimulation. This feature was probably the instruction which required the subject to press the finger button when he was about to feel pain. The increased arm tension of the psychiatric patients probably reflects a heightened preparatory set for finger pressure in these patients.

#### 2. Change in Muscular Tension upon Stimulation

Fig. 2 shows mean arm tension, by clinical group, for each of the four 10-second intervals which

were integrated. Since the integration period represented by point S started simultaneously with the 3-second stimulus, the average tensional response to pain stimulation is represented by the change from points BS to S in the graphs. Inspection of Fig. 2 reveals that the change in tension with stimulation was greatest in the psychoneurotic and acute psychotic groups, intermediate in the control group and least in the chronic schizophrenic group. The figure shows little evidence of any change in tension in response to questioning (change from BQ to Q) in any of the groups.

Fig. 3 shows mean change in arm and neck tension plotted against intensity of thermal stimulation. In general the muscular responses bore a definite relationship to the intensity of the stimulus, the magnitude of response increasing as intensity increased. However, it will be noted that the arm response curve of the chronic schizophrenic group was almost flat, and that the neck curve of this group was also flat, except for the response to the most intense stimulus.

Change in neck muscle reaction was significantly greater in the psychoneurotics and acute psychotics than in the controls. This positive finding should be considered with reference to the negative finding that level of neck tension was not different from group to group. It should also be noted that there was no significant difference between psychoneurotics, acute psychotics, and normals with respect to frequency of overt head-withdrawal.

The differences between these patients and the controls were most pronounced at the lower intensities. In fact, the differences at the higher intensities were not reliable statistically. The tendency for larger differences to occur with lower intensities is particularly evident in the graph for neck potentials, (see Fig. 3).

Present data underline a methodological point which we have made previously,<sup>13</sup> that the stimulation should be relatively *mild*, because overstimulation may obscure critical individual differences in reaction. On the other hand, in the absence of controlled mild stress, such critical differences may not be brought out either.

Data from both arm and neck showed diminished responsiveness to immediate pain stimulation in the chronic schizophrenic group. This group was the only one which displayed a significant divergence between tensional level and tensional change. They manifested a high level of muscular tension in the arm during the whole test, but at the same time showed only a very mild reaction to actual stimulation.

### 3. Relation between Integrated EMG Measurements and Other Measures of Muscular Activity

In our previous work<sup>9, 13</sup> a record of finger movement, similar in kind to that utilized by Luria,<sup>8</sup> was employed. This measure had considerable value in differentiating patients with severe anxiety states from other psychiatric patients and from controls. It was thus important to determine to what extent disturbance in the finger movement record was a function of increased muscular tension. To secure an answer to this question, the finger movement records of the psychoneurotic and acute psychotic groups were scored by a rating method identical to that described previously.<sup>9</sup> By this method, the record was divided into specified time segments and a plus rating assigned to each segment containing a clearly visible elevation from the baseline of finger movement. The sum of the plus ratings so obtained gave an index of finger movement irregularity. Also, the number of button pressures was scored separately and added to the finger movement total to give a total finger movement score.

Two correlations between the arm tension and finger movement data were carried out: (1) The degree of correlation between number of button pressures and change in tension upon pain stimulation was determined. (2) The degree of correlation between mean tension level and total finger movement score was also determined. The product-moment coefficients obtained were  $+0.57$  and  $-0.08$  respectively.

The first correlation ( $+0.57$ ) indicates that, as would be expected, the frequency of voluntary arm response was an important factor influencing the amount of recorded tensional change. However, the correlation was sufficiently small to indicate that the EMG was measuring much more than button pressure. Fig. 4 (A) shows that the EMG could pick up marked tensional change at the time of stimulation (in this case anticipatory tension) even when no button pressure occurred. The second correlation ( $-0.08$ ) indicates that finger movement irregularity was not a function of muscular tension, at least in the present subject group, and that the two measures may be regarded as independent of one another. An example of one kind of independence is illustrated by Fig. 4 (B): the finger movement line might change very little subsequent to button pressure, whereas the EMG might record a prolonged increase of tension.

These results indicate that our previous measure of finger movement cannot be interpreted as a measure of muscular tension. Our finger movement tracings provided a record of *irregularity* in muscular activity, rather than a measure of tension. High irregularity and low tension were found in some cases, while low irregularity and high tension were found in others. It is likely that the finger movement record provides a measure of motor control, and that, within limits, motor control may vary independently of muscular tension.

## II. Rapid Discrimination Test

Mean arm tension values for each group during the Rapid Discrimination Test are shown in Fig. 5. Values are shown for 5 periods: (1) preceding the test, (2) Series I, (3) Series II, (4) Series III, and (5) for the after-period starting 40 seconds after the last series was finished. Fig. 5 shows that tension followed the same general course in all groups. Arm tension rose during the performance period and was generally lower in the after-period than in the pre-test period.

In the period just preceding the test, tension level was about the same in psychoneurotics, acute psychotics and controls. The highest initial tension was found in the group of chronic schizophrenics. The value for this group was reliably higher than that for the controls.

In Series I, and during the after-period, mean arm tension for the controls was reliably lower than that for any patient group, and tension for controls was also significantly different from that for psychoneurotics in Series III. These results indicate that under the stress of this test, greater arm tension was required by the psychiatric patients than by the controls. The persistence of this greater tension in the psychoneurotics after the test (in the absence of an initial difference between psychoneurotics and controls) was an indication of residual tension in the psychoneurotics.

It should be pointed out that actual test performance, in terms of number of correct judgments, was almost identical for the control, psychoneurotic and acute psychotic groups. Therefore, the greater tension in the patients cannot be ascribed to disturbance produced by inferior performance.

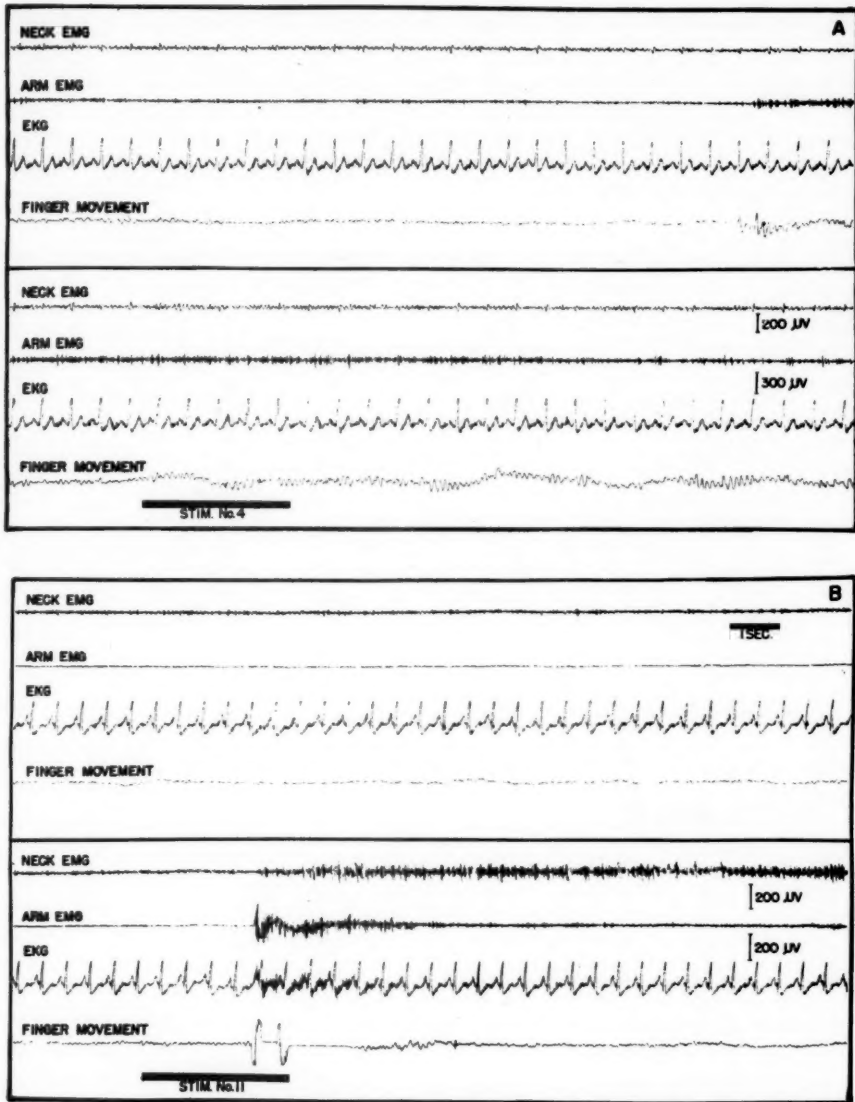


FIG. 4. Photographs of records from Pain-Stress Test. (A) Illustrates marked arm EMG change in the absence of button pressure upon stimulation. Note that change starts in anticipation of stimulus. (B) Shows example of prolonged EMG increase associated with small change in tracing of finger movement following button pressure. Note also marked increase in neck potentials.



The data indicate that, for a performance of equal accuracy, psychiatric patients had to expend significantly more muscular energy than control subjects.

The chronic schizophrenic patients, as a group, had considerable difficulty in carrying out this performance. The schizophrenics were quite variable in this regard. Some achieved very high scores, while others failed to make the required judgments in the time allotted. The curve for the schizophrenic group in Fig. 5 is based upon the 10 patients who were able to perform the test in accordance with instructions.

There were fewer button pressure responses in this group than in any other group. Therefore

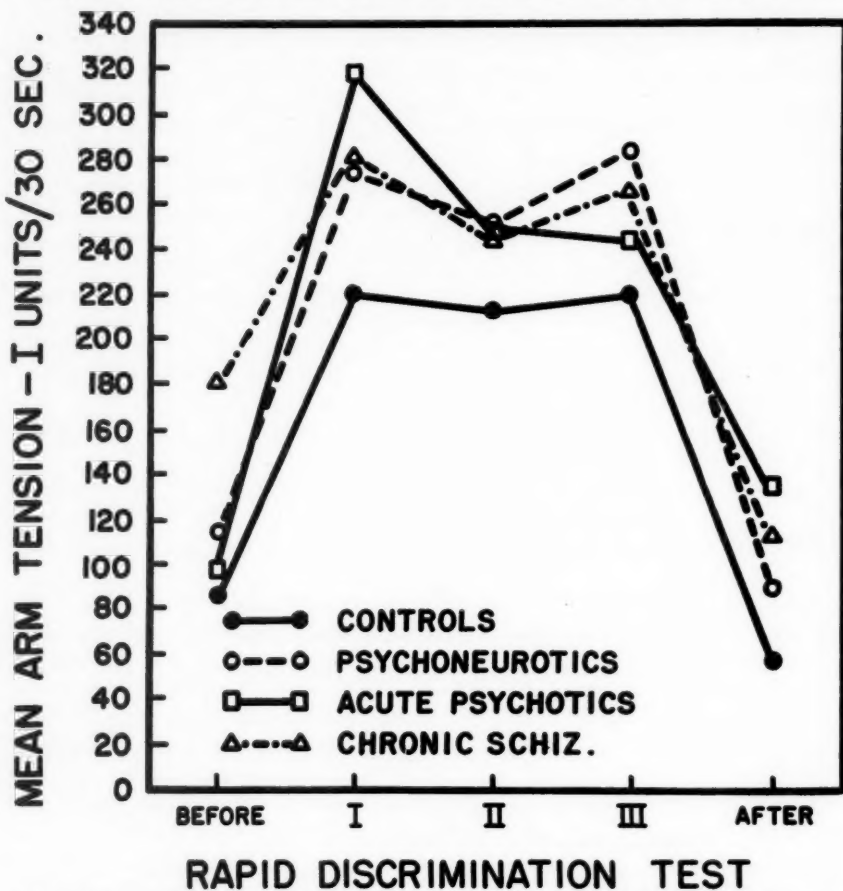


FIG. 5. Mean arm tension during Rapid Discrimination Test. Compare initial contiguity of points for controls and patients with wider separation of the points during and after the test. Note high initial tension in chronic schizophrenics.

the muscular tension levels during performance may be said to be "artificially" lowered. Even with this "artificial" lowering, the tension recorded in the chronic schizophrenic patients was higher than that in the control subjects and as high as that in the other patient groups. Further, the tension in the after-period showed a greater reduction from the pre-test period in the chronic schizophrenic group than in any other. This indicates that the high pre-test tension was probably a response associated with expectation of the coming test for which instructions had already been given.

From our experience with chronic schizophrenics in this test, there is no doubt that it was much more disturbing for them than pain stimulation. This is based on findings with heart rate and blood pressure, and from observing their behavior, as well as on the present muscle tension data. Threat of pain appeared mild in comparison with the threat of being forced into active contact with the environment, into making rapid decisions, and into reporting these decisions verbally to the examiner. These results show that it is hazardous to draw conclusions regarding reactivity in schizophrenia from observations in only one type of stress situation.

### III. Mirror Drawing Test

#### 1. Qualitative Observations

Inspection of the EMG's taken during the mirror drawing tests revealed certain interesting phenomena which were not readily discernible in the quantitative data, because of the long (30 second) periods of integration employed. These were as follows:

(a) "Recruitment" Effect. In the majority of records, the pattern of muscular activity was such as to suggest a "recruitment" of additional motor units as the mirror drawing performance progressed. This effect was visible not only in the EMG from the active arm, but was also frequently observed in the neck EMG (see Fig. 6). The time of maximum "recruitment" varied, but



FIG. 6. EMG tracings taken during Mirror Drawing Test illustrating "recruitment" phenomenon in arm. Note marked increase in neck potentials just before and during mirror drawing.

it occurred most commonly within the first few seconds of performance. In some cases the last second or two of performance was accompanied by maximal bursts of EMG activity. This may be an example of Hull's "goal gradient" phenomenon.<sup>5</sup>

(b) *Anticipatory Tension*. In some cases the maximum increase of EMG activity in the arm occurred a few seconds prior to the starting signal, indicating that muscular tension reached its peak in these cases before the performance was started. In the record shown in Fig. 6, neck activity reached a high level during the instruction period.

(c) *Alternation of Activity between Focal and Remote Areas*. In a number of records a remarkable alternation of activity between the arm and the neck EMG's was observed. A striking example of this effect is shown in Fig. 7, together with a reproduction of the mirror drawing performance. At point X in the drawing, an obvious block occurred, with the pencil nearly going

off the paper in the wrong direction. Simultaneously, there was a marked reduction in muscular activity of the arm. As the arm activity was reduced, there was an abrupt increase of neck activity, which lasted for several seconds while the arm EMG was at a low level. With the resumption of arm activity the neck activity diminished somewhat and then rose toward the end of the performance (recruitment, "goal gradient").

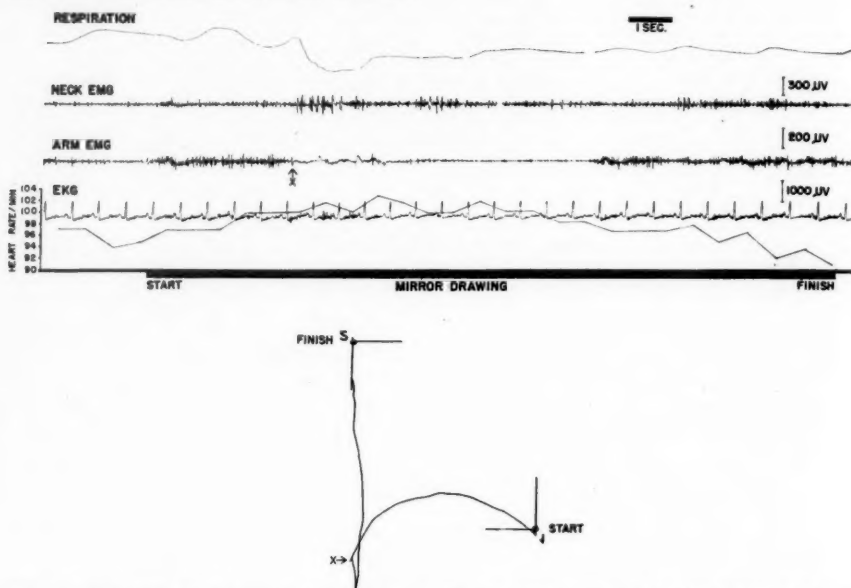


Fig. 7. Record from Mirror Drawing Test illustrating shifts of muscular tension and related change in heart rate, at time (X) when block occurred in the motor performance. Note that when arm potentials decrease, neck potentials increase and muscle potentials (leg) appear in EKG. Note also breath-holding and increase in heart rate at this time.

Fig. 7 shows also that the neck response was not the only example of increased activity in relatively remote body areas during the period of diminished focal (arm) activity. The EKG was a lead II recording taken from one of the EMG right arm leads to a lead on the left leg. Since the arm was quiescent, the muscle activity recorded in the EKG line during the period of reduced arm activity must have come primarily from the leg muscles. Another effect of interest in this recording was the increase in heart rate observed during reduced arm activity (see Fig. 7). This heart rate increase may have been associated with breath-holding, as indicated by the respiratory tracing in Fig. 7.

Inspection of the records taken in this experiment revealed definite evidence of alternation of activity between neck and arm in 11.3 per cent of the first and in 21.2 per cent of the second mirror drawing tests. No further systematic analysis of the records was done, since it was felt that a specially designed experiment would be required in order to study this alternation phe-

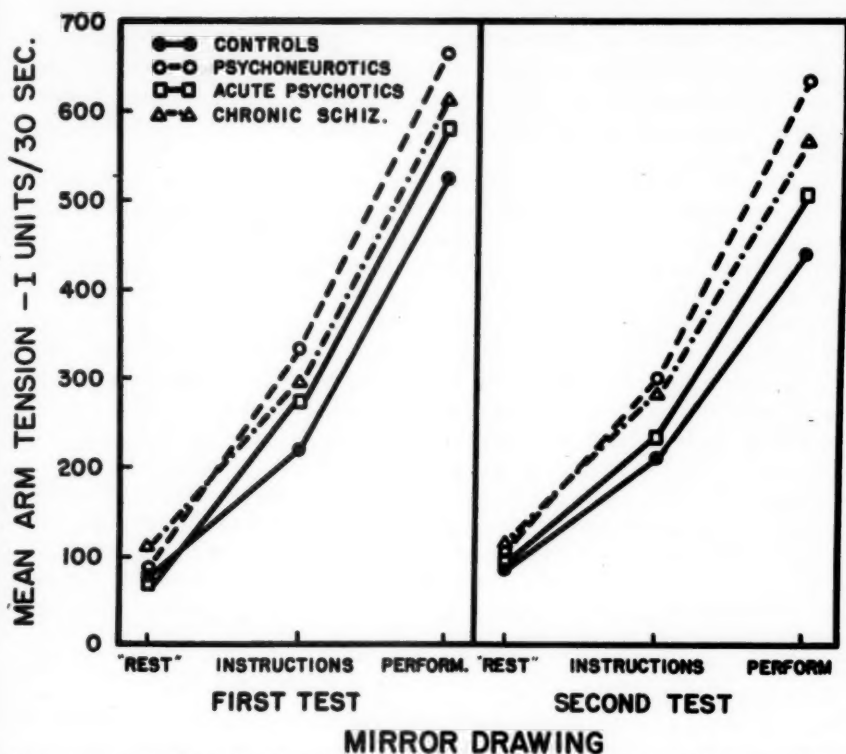


FIG. 8. Mean arm tension during Mirror Drawing Tests. Compare initial contiguity of points for controls and patients with wider separation of the points during instruction and performance.

nomenon adequately. However, the observations reported here serve to indicate that interruption of muscular activity, directed toward a goal, may be accompanied by widespread physiological changes elsewhere, both in remote skeletal muscles and in autonomic effectors. Just which remote areas will be most affected may possibly have an important bearing on the localization of tensional symptoms. In this connection, it is of interest to note that the control subject, whose record is shown in Fig. 7, was prone to frequent, severe headaches, which she recognized as occurring under conditions of emotional strain.

## 2. Quantitative Tension Data

Fig. 8 shows the mean arm tension values for both tests. The curves show the expected general increase of arm tension during instructions (the subject held a pencil in readiness for drawing) and a further large increase during the actual mirror drawing performance. During the "rest" periods, the tension levels of all groups were approximately equal and did not differ reliably from one another. This observation provides strong evidence favoring the methodological assumption

that imposition of stress is required to bring out critical physiological differences between patients and controls. From this finding we may infer that the differences during the non-stimulation periods of the Pain-Stress Test (BS, BQ and Q in Fig. 2) were a result of differential tensional response to the stress situation, and not merely due to ever-present differences in level between patients and controls.

Preparation for activity, during the instruction period, had a differential effect on the groups. In Fig. 8, note the separation of the points representing tension for each group during instructions. Note further that in both tests, psychoneurotic tension was highest and that control tension was lowest. These differences in tension level between psychoneurotics and controls were both statistically reliable. Moreover in both tests the *change* in tension from the rest period to the instruction period was reliably greater for psychoneurotics than for controls.

This finding is, in some respects, similar to that of Ruesch and Finesinger,<sup>15</sup> who showed that grip-pressure on a pencil during the writing of a standard sentence was greater in psychiatric patients than in control subjects. However, the present data differ from those of Ruesch and Finesinger, insofar as no writing or drawing was done during the instruction period.

The points for the two psychotic groups, during instructions, lie intermediate between those for psychoneurotics and controls. In the first test, acute psychotics showed a *reliably* greater change from rest to performance than controls. In the second test the corresponding change was not reliably greater in the acute psychotics. As a matter of fact their change was *reliably less* than that of the psychoneurotics. Moreover the comparison of these two groups in *level* of tension during instructions also yielded a reliable difference in the direction of higher tension in the psychoneurotics than in acute psychotics.

Tensional reaction by the chronic schizophrenics in this test was, again, unexpectedly high. In the second test tensional level was reliably *higher* than that of the controls.

The same group rank order for tension was maintained in going from instruction period to the period of performance (see Fig. 8). However, no reliable differences between groups were found in amount of tensional change in going from instructions to performance. There was only one reliable difference between groups for the performance period: on the second test *level* of tension was reliably higher for psychoneurotics than controls. These statistics indicate that the condition of preparation for activity was more differentiating between patients and controls than the actual performance. There was the further indication that the preparatory period preceding performance was more productive of tension in psychoneurotics than in acute psychotics.

#### IV. Consistency of Muscular Tension in Different Stress Situations

The employment of more than one stress situation made it possible to determine degree of individual consistency in muscular tension from one stress situation to another. An estimate of individual consistency in muscular tension may be gained from a statistical study in which the tension scores are correlated with one another. Correlations were carried out with the subject population composed of the 49 cases from the psychoneurotic and acute psychotic groups, for whom all arm tension scores were available. Since these groups represented an unselected heterogeneous hospital population it was felt that employing them for correlational purposes would yield a reasonably meaningful result. Two sets of intercorrelations between the tension

values determined in different stress tests were calculated, as follows: (1) Non-active periods (mean values for the integration preceding the pain stimulus and for the "rest" periods preceding Rapid Discrimination and Mirror Drawing), (2) Active periods (mean values for integrations covering the pain stimulus and the performance periods of Rapid Discrimination and Mirror Drawing).

TABLE III  
*Intercorrelations Among Arm Tension Levels in Different Stress Tests\**

Stress Test	Non-Active Period			Active Period		
	R.D.	M.D.I.	M.D.II	R.D.	M.D.I.	M.D.II
Pain-Stress	.66	.33	.31	.81	.48	.47
Rapid Discr. (R.D.)		.33	.39		.52	.56
Mir. Draw. I (M.D.I.)			.28			.69

\*For 49 cases, the minimum correlation for statistical reliability at the 5% level of confidence must be 0.28; for the 1% level of confidence, a coefficient of 0.36 is required.

Table III shows that the highest correlations were found during the active periods of the stress situations. As might have been expected, the degree of consistency was higher between tests in which the activity of the arm was similar than in those where it was not. For example, the correlations between Pain-Stress and Rapid Discrimination were higher than those between either of these tests and Mirror Drawing, whereas the two Mirror Drawing Tests, during the active period, correlated better with one another than with either of the other stress tests.

When one considers the variety of activities in which the arm muscles were engaged, the data indicate a remarkable degree of consistency in muscular tension from one stress test to another. There seemed to be a general factor for muscular tension in the individual, such that some individuals consistently showed higher tension than others. It appears that this factor may become particularly evident during active performance. Further evidence in support of such a factor was found by correlating the mean arm and neck tension values found in the Pain-Stress test. The coefficient was small, but statistically reliable (+0.36), indicating a tendency for high neck and high arm tension to be associated.

#### DISCUSSION

The present data provide objective confirmation of the widely held clinical impression that muscular tension tends to be abnormally high in psychiatric patients.<sup>1</sup> This excessive muscular tension is probably of considerable importance in the production of symptoms. Since ordinary situations in everyday life may evoke stress-reactions in psychiatric patients, such reactions attended by abnormally high muscular tension, surely must occur with high frequency. The relatively large expenditure of muscular energy involved may account, to a considerable extent, for the common complaint of general fatigue among these patients. Localized somatic symptoms may also be accounted for in terms of excessive muscular tension. Specific tensional reactions to stress have been observed in the neck in association with proneness to headache.<sup>10</sup> Malmö, Shagass, and F. H. Davis<sup>11</sup> reported the case of a patient who complained of a "tired feeling" in the head when sensitive material was being discussed in psychiatric interview. The subjective complaint was preceded by a sustained burst of high-level electromyographic activity from the frontalis muscle. We have since observed a case in which complaint of head discomfort during interview was preceded by a similar burst of muscle potentials from the neck.



We may now proceed from this finding of generally increased tension in the patients, to the results from finer analysis of the stress situation. The data from the Mirror Drawing Test were particularly useful for such an analysis, because of the ease with which the total sequence could be divided into: (1) "rest" period, (2) preparatory period (instructions), and (3) performance period. When the data from the Mirror Drawing Test were fractionated in this way the most reliable tensional differences between patients and controls were found in the preparatory period.

It is interesting to compare our data from recording muscular tension in this test with the data obtained from simultaneous recording of blood pressure and heart rate. Both patients and controls evidenced a marked rise in blood pressure and heart rate during the preparatory (instruction) period of the test, and the rise was approximately equal in the two groups. Contrariwise, the rise in muscular tension observed during the instruction period was considerably greater in the patients than in the controls. These findings seem to indicate an approximately equal *autonomic* preparatory response in patients and controls, accompanied by a greater *somatic* (skeletal muscle) preparatory response in the patient groups. Evidence for excessive tension in preparation for activity was also noted in the Pain-Stress Test. These facts suggest that in psychoneurosis there may be a defect in some regulatory mechanism in the skeletal-motor system, such that immediate tensional output is too great. A not dissimilar conclusion was reached by Luria,<sup>8</sup> and a possible central nervous system regulatory mechanism in which the defect may lie, has been suggested by Malmo, Shagass, and J. F. Davis.<sup>12</sup>

These considerations add further weight to the argument that the skeletal-motor aspect of emotional states is an important one, deserving more attention than it has heretofore received. In the relatively few studies which have dealt with skeletal reactions in emotion<sup>8,9</sup> *irregularity* of finger movement was employed as a measure. In the present investigation no correlation between this measure and the measure of total forearm tension was found. This absence of correlation indicates that these two measures represent independent aspects of muscular activity, both of which tend to be high in psychoneurosis. Excessive irregularity of activity may be found in the presence of low muscular tension, perhaps partly on the basis of frequent movements of the ballistic type described by Stetson and Bouman.<sup>10</sup> Such a patient might display considerable fidgetiness and jumpiness, yet his actual level of muscular tension might be within the normal range. On the other hand, a patient appearing relatively immobile might, upon objective measurement, be found to show a very high level of muscular tension; this immobility could be achieved through co-contraction of the antagonistic muscles. In the present study, one patient with psychoneurotic depression appeared, clinically, to show considerable motor retardation, yet the EMG revealed a very high level of muscular tension.

Another instance of the importance of making the distinction between a measure of level and a measure of change, was noted with reference to neck muscle contraction in the Pain-Stress Test. Psychoneurotics differed from controls in *change* (showing significantly greater change upon stimulation) but the two groups did not differ significantly with respect to *level* of neck tension (total tension during entire test). This finding adds further support to the hypothesis advanced by Malmo and Shagass<sup>9</sup> that one of the distinctive characteristics of psychoneurotic anxiety is that of over-reaction to stimulation.

There is the further implication that while over-reaction during the phase of preparatory set

may be localized (e.g. in a high level of right arm tension in the Pain-Stress Test) the over-reaction may become more generalized during stimulation (e.g. greater than normal change in both neck and arm). It would appear that the deficiency in the psychoneurotic's C.N.S. regulatory mechanism<sup>12</sup> may be most evident under conditions of actively changing sensory stimulation.

The high inter-test correlations suggest that there may be a basic physiological factor of muscle tension in personality. Freeman has suggested that there may be such a factor (4, p. 258). However, in the factorial studies of physiological variables which he cites, no direct measurements of tension, in terms of muscle potentials, were made.

Finally we come to the results from the chronic schizophrenics whose relatively high muscular tension in certain situations was surprising, considering the widely held view that schizophrenia is characterized by physiological unresponsiveness.<sup>6</sup> In their immediate response to pain stimulation, these chronic schizophrenics were unresponsive, relative to the other groups. But in the other two stress tests, their tensional reactions resembled those of the psychoneurotics and acute psychotics.

Defense against mild pain stimulation in the schizophrenics was low, while responsiveness in situations demanding active performance on their part was remarkably high. Focusing on the physiological measures, background or tonic reactivity was in no instance observed to be significantly lower than normal, and in the Pain-Stress Test, in spite of low frequency of button pressures, level of tension in the arm was significantly higher than normal (as high as that of the psychoneurotics). This seemed to represent a typical schizophrenic split between attitude and reality. The high arm tension appeared to represent a strong preparation for defense against pain; but when the pain came the actual defense reaction was weak.

From a strictly physiological point of view no general reduction in capacity for reaction was seen in the chronic schizophrenics whom we studied. Their poor social adjustments do not appear to be due, therefore, to any such basic physiological deficiencies.

Comparing these results with those which Malmö and Shagass obtained with early schizophrenics, we note a decided difference between early and chronic schizophrenics. The much lower reactivity of the chronic schizophrenics is evidence for a trend toward lowered reaction to pain as schizophrenia progresses toward chronicity. However, present data indicated that such a trend toward lower reactivity is probably specific to an experience like pain, and may not obtain in other situations, such as performance tests.

### SUMMARY

1. Electromyograms from the flexor muscles of the forearm and from the neck muscles were recorded from 75 psychiatric patients and 21 normal controls in three standard stress situations. The patients included 44 psychoneurotics, 14 acute psychotics and 17 chronic schizophrenics. The stress situations involved: (a) pain stimulation; (b) a speeded size-discrimination task, and (c) two mirror drawing tasks. The muscle action potentials were quantified by means of an integrating device which was validated in experiments employing a dynamometer as an independent measure of muscular tension.

2. The results and main conclusions may be summarized as follows: (a) Psychoneurotic and psychotic patients responded to stress with a greater degree of muscular tension than that found

in control subjects. This finding, which was consistent for all three stress situations, was discussed in relation to the common clinical findings of fatigue and specific tensional complaints in psychoneurotics. (b) Data obtained from simultaneous recording of blood pressure, heart rate, and EMG's in the Mirror Drawing Test showed an approximately equal autonomic preparatory response in patients and controls, accompanied by a greater somatic (skeletal muscle) preparatory response in the patient groups. This finding was discussed in relation to the question of central nervous system regulation of somatic activities. (c) No significant relationship was found between degree of muscular tension in the forearm flexors and degree of irregularity of motor activity as observed in a record of finger movement, indicating that measures of muscular tension and measures like the "Luria tremorgram" represent independent aspects of muscular activity. (d) There was considerable individual consistency of muscular tension from one stress situation to another. This finding supports the claim for a factor of muscular tension in personality. The greatest degree of consistency was observed during periods of active stress stimulation, even though the motor activities involved were quite dissimilar. (e) Level of muscle tension was as high in schizophrenics under stress as in other psychiatric patients, but the schizophrenics were tensionally hyporeactive to pain stimuli of brief duration. Since their tensional responses in other situations (particularly those calling for active participation) was not diminished, it was concluded that there was no general reduction in capacity for physiological reactivity.

#### ACKNOWLEDGMENT

We wish to acknowledge the invaluable assistance of Mr. D. J. Belanger, Dr. G. A. McMurray and Dr. A. A. Smith in taking the data and in the statistical analysis.

#### RESUMEN

1. Se ejecutaron electromiogramas de los músculos flexores del antebrazo y del cuello en 75 pacientes psiquiátricos y en 21 testigos normales, sometidos a tres situaciones típicas de tensión y esfuerzo. Los pacientes incluían 44 psiconeuróticos, 14 psicóticos agudos y 17 esquizofrénicos crónicos. La situación de tensión comprendió: a) estímulo dolorígeno; b) prueba acelerada de diferenciación de tamaño; c) dos problemas de dibujo en espejo. Se midió el potencial de la actividad muscular mediante un dispositivo de integración cuyo valor fué confirmado en los experimentos empleando un dinamómetro como medida independiente de la tensión muscular.

2. Los resultados y conclusiones principales se pueden resumir del modo siguiente: a) Los pacientes psiconeuróticos y psicóticos respondieron a la tensión y esfuerzo con un mayor grado de tensión muscular que aquellos que sirvieron de testigos. Este resultado, que fué común a las tres situaciones de esfuerzo y tensión, se estudió en relación con los datos clínicos de fatiga, y las quejas específicas de tensión por parte de los pacientes psiconeuróticos; b) los datos obtenidos de trazados simultáneos de la tensión arterial, frecuencia del latido cardíaco y EMG en la prueba del dibujo en espejo, demostraron una respuesta autonómica preparatoria aproximadamente igual en los pacientes y testigos, acompañada de una mayor reacción somática preparatoria (de los músculos esqueléticos) en el grupo de pacientes. Este resultado se ha estudiado con respecto a la regulación de las actividades somáticas por el sistema nervioso central; c) No

se encontró una relación notable entre la medida de la tensión de los flexores del antebrazo, y el grado de irregularidad de la actividad motora, como se observó al registrar el movimiento de los dedos, que indique qué medidas de la tensión muscular, o medidas tales como el "tremograma Luria," representan aspectos independientes de la actividad muscular; d) se observó una notable consistencia individual de la tensión muscular, entre una y otra situación de tensión y esfuerzo. Esta observación favorece la idea de que existe un factor de tensión muscular en la personalidad. El mayor grado de consistencia se observó durante los periodos de intenso estímulo de la tensión muscular, aun cuando las actividades motoras comprendidas fueran completamente diferentes; e) la tensión muscular en los esquizofrénicos fué igual a la de otros pacientes psiquiátricos, pero los esquizofrénicos fueron *tensionalmente* hiporreactivos a los estímulos dolorosos de corta duración. Como las reacciones de tensión en otros casos (particularmente en aquellos que requerían una participación activa) no disminuyeron, se llegó a la conclusión de que no había una reducción general de la *capacidad* para la reactividad fisiológica. La capacidad de reaccionar en la esquizofrenia parece depender de la naturaleza de la tensión.

## RESUME

1. On a pris des électromyogrammes des muscles fléchisseurs de l'avant-bras et des muscles du cou sur 75 sujets psychiatriques et 21 sujets normaux de contrôle dans trois situations de tension courantes. Les sujets étudiés comprenaient 44 psychoneurotiques, 14 psychotiques aigus et 17 schizophrènes chroniques. Les situations de tension mises en oeuvre consistaient en: (a) stimulation à la douleur; (b) une tâche de discernement rapide des dimensions, et (c) deux tâches de dessin au miroir. Les potentiels de l'action musculaire ont été mesurés au moyen d'un appareil intégrateur dont les résultats ont été confirmés par des essais utilisant un dynamomètre comme mesure indépendante de la tension musculaire.

2. Les résultats et principales conclusions de ces essais peuvent se résumer comme suit: (a) Les sujets psychoneurotique et psychotiques ont réagi à la tension par un degré plus prononcé de tension musculaire que chez les sujets normaux de contrôle. Cette constatation, qui a été faite pour la totalité des trois situations de tension, a été étudiée par rapprochement avec les observations cliniques courantes relatives aux tensions particulières et fatigues dont se plaignent les psychoneurotiques. (b) Les observations faites par l'enregistrement simultané de la pression artérielle, des battements du coeur et de l'EMG dans l'Epreuve de Dessin au Miroir ont révélé une réaction préparatoire autonome sensiblement égale chez les sujets malades et chez les sujets de contrôle, accompagnée d'une plus forte réaction préparatoire somatique (muscle squelettique) chez les groupes des sujets malades. Cette constatation a été étudiée en relation avec la question de la régularisation du système nerveux central des activités somatiques. (c) Aucune relation significative n'a été observée entre le degré de tension musculaire dans les fléchisseurs de l'avant-bras et le degré d'irrégularité de l'activité motrice telle qu'observée dans un graphique du mouvement du doigt, faisant ressortir que les mesures de la tension musculaire et les mesures telles que le "crispogramme Luria" constituent des aspects indépendants de l'activité musculaire. (d) On a observé un degré remarquable d'uniformité individuelle de la tension musculaire en passant d'une situation de tension à une autre. Cette constatation confirme la prétension d'un

indice de tension musculaire correspondant à la personnalité du sujet. Le plus haut degré d'uniformité a été observé au cours des périodes de stimulation active de tension, bien que les activités motrices en jeu se sont montrées très dissemblables. (e) Le degré de tension musculaire s'est montré aussi élevé chez les sujets schizophrènes sous tension que chez les autres sujets psychiatriques, mais les schizophrènes se sont montrés tensionnellement hyporéactifs à l'égard de stimuli de douleur de courte durée. Etant donné que leurs réactions de tension dans d'autres situations (en particulier celles demandant une participation active) n'étaient pas moindres, on en conclut qu'il n'y avait pas de réduction générale de la *capacité* en réactivité physiologique. La réactivité en schizophrénie semble dépendre de la *nature* de la tension appliquée.

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# The Social Psychopathology of the Schizophrenic States

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As we know, the mental life of the individual is in constant contact with that of others. There is a continuous process of mutual giving and receiving. This, surely, is the fundamental form of every kind of mental activity.

We should, therefore, expect that psychiatry, which is the study of disturbances and defects in the mental life of the individual, should also be interested in the consequent disturbances of the mutual relationships between human beings.

However, this has not been the case. We have seen sporadic attempts, to begin with, from French quarters: Emile Durkheim, Charles Blondel, Pierre Janet. In America especially, William White and Frankwood Williams have more recently advocated the sociological view of psychiatry. More systematic social psychiatric investigations have been carried out by Malzberg and Pollock and Dayton.

In Scandinavia, especially Oedegaard, Braatøy and Aamark have gone more deeply into the problems. But broadly speaking, the interest must be said to have been but slight.

To our regret we must agree with Henry Maudsley when he says in his book "The Pathology of Mind" (1895): "The study of the individual as an element of social pathology will plainly be a long, laborious and difficult business of the future."

When we chose to deal with the social psychopathology of the schizoidias and the schizophrenias, we had two reasons for it. First, the social-psychiatric views play, on the whole, too subordinate a part in the schizophrenia problematics of today and second, because, perhaps, these very conditions make us see most clearly the value of sociological thinking in psychiatry, as in many ways they occupy an extra-position sociologically. This has been demonstrated by Dayton and Oedegaard in their statistical investigations of marriages, by Braatøy through his study of men between 15 and 25, by Arnesen, Melsom, Oedegaard and others in their investigations of emigration, and by Dunham in his ecologic investigations.

In this paper, however, we shall not go too much into statistical detail. Our view will be one of clinical sociology. In our analysis we will endeavour to relive the social correlations of these men, try to find common features which may possibly explain their sociological situations, and thus throw light upon the ever burning question of heredity and environment.

But before we enter upon our actual task, we shall have to give a very brief orientation on social psychology.

Even Aristotle saw the need of men to come into contact with one another, and called man a social animal. That is to say that the psychophysical unity, man, is in possession of both an I-consciousness and a we-consciousness. This social ability is original, i.e. as immature in the little child as the other elements of personality. It is developed on the basis of the social contact impulse through a socialization process, a social integration. The active forces in this process are of an inner personal as well as of an outer social kind. The result is that the individual

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is bound to totality by means of totality, which again constantly influences each separate component. Different forms of dependence between the self, him, her and them arise. And the degree of this integration can be measured by the need and the power for cooperation.

It is the relations of this social integration and of its contrast, the desocialization, social disintegration, which form the background of our considerations.

When we now enter upon our special task it may be useful, to begin with, to adopt a more general view of the contact impulse, so that we consider human intercourse in general, thus paying no regard to the more special social situations. The social norms we shall then have to deal with will be the more elementary ones, such as approach, politeness and decency. These are relations which we know are based on mutuality; accordingly, a principle of resonance, the parts involved both giving and receiving.

R. V. Jhering, who has been engaged very much in the study of these problems, sets up in this connection, among others, the following radicals: The turning to another person, the bow, the handshake and the phraseology, and, we may add, the posture and the mimicry.

Let us look more closely at the relations of these conditions in the group of men we are studying.

Even the posture tells us much. When an individual approaches another, a change of posture takes place as a rule. It becomes more bent, obliging. This often does not occur in our individuals. Their posture is stiff, the movements often few, not particularly supple, clumsy, disharmonic, with the impression of self-consciousness. The person often gives the impression that he does not want to be approached. He turns his head aside, and it is difficult to catch his eye.

Similarly, the bow is often stiff, clumsy, reserved, and in the schizophrenics it often disappears completely. Mimicry is poor, the face often serious, without any smiles, or the smile is frequently a shy one with little heartiness in it. The inadequate smile is also often found. This can be a normal phenomenon during puberty, but it usually disappears with the years. In our type of man, however, this can persist, as they often stagnate at the juvenile stage.

The mimic movements of expression are like the other movements, abrupt and clumsy. In this connection we remember Kraepelin's words about the lack of grace of the schizophrenic.

Furthermore the handshake is often characteristic because of its extraordinary laxness, a relation often pointed out by Vogt. The phraseology is also often submitted to changes. Phrases of welcome and departure often disappear in the schizophrenic. The form of address can often be submitted to peculiar changes, often with a tendency to the impersonal with application of the third person. The language of schizophrenics assumes on the whole very peculiar and completely incomprehensible forms through the so-called neologisms. This field is very little investigated and should interest philologists as well as psychiatrists.

These are the phenomena which can be observed objectively, and which are interesting enough. But we must go further in our research. As mentioned before we must try to penetrate into the psyche of these men so as to see the structure of their personality in relation to their outward social behaviour. This relation is of great importance, especially for the understanding of the term schizoidia.

The decisive criterion for the application of this term must be the contact feeling, which must always be evaluated. In psychiatry we have a number of conditions which apparently indicate schizoidia, because of introversion and isolation. They may be neurotically conditioned:

erythrophobia, neurotic homophobia, different depressions, etc. But these ailments differ in essential ways from the schizoidias in social-psychologic respect.

The first-mentioned ailments are not characterized by a lack of contact feeling; there is, on the contrary, a pronounced contact hunger. There is no homophobia in the ordinary sense. The phobic fear of social contact is often the result of the fear of not being able to meet with the usual conventional demands with regard to sociability. From this comes the fear of not being able to master language, movements, mimicry, etc. and thereby becoming socially outcast. Patients on whom isolation has been forced feel this as a great disaster.

In the schizoidias, however, there is usually a weakening of the contact wish, the contact impulse, to partial obliteration as in schizophrenic autism. They have a reduced or almost extinct social need. They are usually pleased in their isolation. In this connection it is also interesting to notice that if for some reason or other they take to alcohol, they remain as a rule, typical solitary drinkers.

But besides this reduction of contact we often find the purely negative relation, a pronounced contact hostility, an aversion against fellowmen, primary and incomprehensible. Usually it has nothing to do with ordinary antipathy. It represents homophobia in the actual sense and concerns man as a psychophysical unity. Very peculiar are the explosion-like exacerbations of this homophobia, a relation rarely seen in incipient schizophrenia. The homophobia can develop into unbearableness, and be accompanied by violent hot fits and a mixture of undefinable fear and irritation and may end in panic-like flight from either a party or an assembly. This hostile attitude may also come out in an almost uncontrollable desire to beat, spit, scold and mock whatever man they are facing.

The extreme of this phenomenon can be seen in some schizophrenics with explosive attacks of excitement of a catatonic nature. After the attack of excitement is over they may often plead as the cause of this the intolerable sensation of accumulation of tension which the presence of other people may produce in them. A violent discharge is required to loosen this painful condition.

In this connection it may be interesting to mention Karl Wilmann's investigations of murders committed during the initial stage of schizophrenia. For here, as a rule, the motive proved to be the intolerable condition of mental tension of the perpetrator, a tension which required an act of violence for discharge. The relief, the peculiar indifference to the bereaved, is in its peculiarity a very dismal sight, says Wilmann. Criminality, however, is, as we know, rare among schizophrenics, a fact pointed out by Gruhle and Birnbaum and others.

With regard to the emotional explosions it must be mentioned that they also, of course, can have another genesis. Many schizoidias are often pronounced complex beings, a fact that may result in abrupt explosions.

Before we finish the more general survey of the contact reduction, we will mention another feature of these individuals which may make adaptation difficult. It is their tendency to the "splitting up" of fellow-men. They concentrate their attention on some separate part of the body, an eye, a finger, the nose, etc. They no longer have any eye for totality, and this gives them a macabre feeling of disharmony and irritation.

A similar feeling of change of proportion is also observed in some patients with regard to

their own body in the form of so-called cenestopathia. Both of these phenomena can be of a neurotic nature, but much accounts for the assumption that these phenomena are the expression of an incipient schizophrenia.

Thus we see that our group of men objectively as well as subjectively show defects in their capacity to adapt themselves and evidence difficulty in getting used to their fellowmen regardless of what their situation in life may be. We then turn to look at these our fellowmen in more specific sociological situations. It is natural that we start with the family, the basic social situation.

The basis of the family may be said to be the need of sexual and social companionship and the desire to live in relatively controlled and protected surroundings. Both the instincts of self-protection and of family-protection find their natural expression in the family as a social institution.

We will first deal with the situation of the conjugal partners. The basis of this is the highest form of integrated sexuality, a normal or approximately normal sexual synthesis in which the separate sexual radicals are incorporated in a higher unity.

Moll maintains that the basis of sexual life is the detumescence impulse on one hand, and the contraction impulse on the other, i.e. the need for approach to another individual. According to Moll this need is most often of a heterosexual nature, and the two impulses operate most often parallel to each other.

Now, if we ask: how does the sexual life of our type of men appear? we must immediately answer that it deviates from the normal in many and essential ways. Briefly it can be said that these individuals lack the ability to develop the power of contraction, but often have a certain degree of retained detumescence impulse, a relation which, as we know, often dominates the sexuality of the infantile and juvenile stages.

The defective contraction brings about an incomplete sexual synthesis, which particularly affects the last component, namely the choice of the one sexual partner. Therefore, in our type of man, we often meet a striking coldness and indifference to the other sex, and if alliances are initiated, they very often retain a fortuitous character. Or they are satisfied with surrogate-satisfaction such as masturbation, which usually persists far beyond what is normal. In the schizophrenics there also seem to be less fanciful phantasies during masturbation than in normal persons. Masturbation is to them more a physical action than an erotic experience. The extreme form of this relation is seen in the completely coercive and forced masturbation, which is certainly essentially based on the detumescence impulse.

The borders on the normal here are naturally extremely difficult to tell with certainty, and the problem must first of all be estimated with due regard to age.

But even if there is a certain degree of contraction we are often struck by the unpractical and utterly helpless behavior of these men. They very often lack the power of realizing the wishes of their dreams. They never get out of the juvenile stage with its masturbation, admiration from a distance, and conceitedness. In the schizophrenics this wrong-judging tendency is mixed up in these relations, and the consequence of this, imaginary sweetheating, is a very frequent feature in the sexual pathology of the schizophrenics.

The stagnation of these individuals on a sexually lower level can also be observed in other ways. Thus a fixation to the homosexual radical is not infrequent. On the other hand, a re-

gression to this level can be seen during the schizophrenic process of disintegration. In this connection we will also notice that it is remarkable how often the wrong-judging tendency in the paranoid syndrome is marked by the accusations of homosexuality. This phenomenon can possibly be regarded as a projection outward of the latent or more or less manifest homosexual tendencies. We have observed the same with pedophilic tendencies, although far more seldom.

As we understand the sexual life of these individuals, it is in many ways defective, and defective contraction is the main feature. This is most clearly seen in the low percentage of marriages among male schizophrenics, a relation pointed out by Oedegaard and Dayton.

As mentioned above, the borders on the normal are vague. Often, of course, families are formed. But on studying these marriages more closely, we shall find as a rule, deviations from the normal. Quite frequently a striking difference of age between the conjugal partners is found. Or we shall see mesalliances and distinct (pronounced) patriarchal and matriarchal alliances.

The development into such conditions depends, of course, on several factors, first of all on both the conjugal parts. In psychiatry, however, we are most frequently faced with these problems when the male partner is the psychically suffering one in schizoid or schizophrene direction. The development takes a somewhat different course in accordance with the asthenic or sthenic direction of the mental tendency.

To understand this we must look a little at the mental change which takes place during puberty, and which is of importance for the whole subsequent social life. During this period the previous subjective, egocentric and absolutistic attitude gradually gives way to the more objective, reciprocal and relative one.

It is exceedingly interesting that our individuals lack to an essential degree this change in their attitude of life. Both the above-mentioned forms of schizoidia retain a pronounced subjective and egocentric character. But the asthenic form is usually of a more sensitive, "mimosa-like" character and in possession of much less absolutism and ambition than the sthenic. Therefore in his marriage the asthenic is as otherwise in life, more submissive and passive in his egocentricity and isolation than the sthenic.

The sthenic has and insists on having absolute power. But because of his barrenness, his defective personality, he lacks the rich radiating inner power which immediately makes a man dominate men. Herbert Spencer says that those influences on men which have a much deeper origin than words and which are exercised without being conscious of it, are the most powerful and, in given situations, the most weighty. Therefore the sthenic schizoid psychopath usually develops only external power. Characteristic of him are opinionativeness, narrowmindedness, lack of a sense of proportion, lack of a broadminded attitude of life, lack of consideration for others and of discrimination. We have before us a special type of the domestic tyrant, the cold schizoid family father, who is quite frequent in psychiatry.

We shall now turn to the child-parent situation. In the family the child is brought up in social habits and to ideal social thinking. Social cooperation will depend on the model situations given by the parents to the children in the form of the first adaptations. The relation is characterized by an incorporation principle, an obedience preparedness on a voluntary, obvious basis. Therefore McDougall reckons this will to abasement among the instinctive equipment, and calls it The Instinct of Abasement. In childhood, the relationship between parents and

children is therefore very strong and intimate, marked by piety, authority and acknowledgment of superiority.

During the age of puberty a partial breach in this relationship takes place. The accustomed family ties are to be loosened so that the young individual may get a more independent extra-familial training. Normal-psychologically this solution takes place in certain schizothymic forms under a certain spite and opposition, introversion and isolation in the form of the so-called negative phase or the second age of defiance. Usually this process takes place with a certain moderation, and without any great difficulties the development goes over into the positive, liberating phase, the so-called second birth of the personality, which forms the introduction to the more independent social life of the individual.

Again turning to the special type of man with which we are dealing, we shall first mention the fact that several workers are of the opinion that a grouping according to type *ad modum* Kretschmer can be made to a certain degree even in school age. The purely individual deviations, however, seem to be much more remarkable than the purely social ones.

Therefore, we shall only deal with the more pronounced, defective social conditions, which we first find during puberty. Thus we shall have to deal with schizoidia, hebephrenia and heboidia. The latter may be said to occupy a medium position between the two first-mentioned deviations.

It is exceedingly interesting to notice that these ailments very often develop together with the normal schizothymic phase during puberty. This relation is of special interest in hebephrenia, which in our present terminology may be designated as a classical form of schizophrenia, for it shows the great importance of the socialpsychologic factor in the development of the schizophrenias.

In a sociological respect, these puberty phases are characterized mainly by the increased and partly uncontrolled breach with family solidarity, either in a form of an isolation, or even more frequently, in the form of an isolation and opposition. And the phenomenon must be said to be of a nature far exceeding the normal juvenile attitude of spite. Especially peculiar and interesting is the family opposition, completely incomprehensible and without motive as it seems to be. Even if applying Freud's and Suttie's jealousy-models and other psychoanalytic methods, it cannot be properly understood. But this peculiar family-opposition is seen not only in these puberty-conditions. It may also be a typical feature during the development of other forms of schizophrenia in later age.

Turning to the extra-familial social life of the late puberty individuals, we first concentrate on friendship, which is a highly important and valuable phenomenon of integration. Friendship is distinguished from comradeship by a more specific selection. Comradeship is essentially based on a more ordinary feeling of fellowship, a group-feeling. As the social need is developed, more personally founded relationships are required, based on mutuality, kindness, love, thus more special mental harmony in the way of feeling, thinking and action. The general concord, however, need not be absolute. Very often more expletive tendencies may prevail. As we understand it, deeper and profounder personality-experience and contact-feeling are required. After what we have learnt about defects in our individuals in these fields, we understand that a certain isolation will ensue even here. But as emphasized above, the phenomena are not absolute.

Indeed, certain attachments may arise, but inadequacy is often encountered as in the marriages:

difference of age, and mesalliances of friendship. The nature of the schizoidias and the sexual equipment also seem to play a part here.

In connection with friendship it is also natural to inquire into the attitude of these types of men to religious life. For, as Vogt says, psychologically the religious way of feeling represents a higher form of society-consciousness. Fellowship and fellow feeling with the superior fellow bring about a mutual mental communication.

The religious feelings of the schizoidias and schizophrenics has been little investigated but, judging from our experience, there can be no doubt that in these individuals there are deviations also as regards this highest form of fellow feeling. As demonstrated by Oedegaard the schizoidias and the schizophrenics show little power of joining religious communities. If they do, they often show in their religious life narrowmindedness and sectarianism and fanaticism.

Schizophrenics seldom have any deeper feelings indicating a richer religious life. Here they distinctly differ from other endogenous mental sufferings, where the anxious, depressive elements are dominating.

On the other hand peculiar religious regressive phenomena are often found in schizophrenics, a regression to the mystic, the magic level, whose outstanding characteristic is egotism and egocentricity. The help of the powers is here sought for selfish purposes, while true religious life is more marked by the altruistic, farseeing mind. Storch has analogized this regression in schizophrenics with the archaic way of thinking of the primitive peoples. But here opinions differ greatly.

The fact, however, remains that in no other mental suffering is there such a pronounced and such frequent magic way of thinking as in schizophrenia. Especially peculiar and characteristic are their mystic experience of the struggle between good and evil, an experience which distinctly differs from the mental agonies of, e.g. the melancholiac, during his experience of God's and Satan's struggle for man.

It should now be clear that the processes of individualization and socialization, broadly speaking, take place parallel with constant overlappings according to the principle of "penetration reciproque."

The clearest expression of this is the development of the instinct to make one's own living which begins to take form in late puberty. Playing, the functional tendency of the child which is extremely subjective, egocentric, striving for sham goals, is replaced by the final instinct for making one's own living, which is far more complicated. It represents the creative, productive process including on the one hand the individual need for independence and self-assertion, and on the other hand the will to produce, to create, to do something useful, together with a feeling of responsibility and the heterosexual family-forming tendency.

Out of this complicated operation of forces emerge three main radicals: self-assertion, will of power, and consciousness of social responsibility. These three social impulses are, through mutual penetration, integrated into the higher, final, social phenomenon: the need for making one's own living.

We understand immediately the importance of the will for power and the consciousness of social responsibility. It may be different as regards the feeling of self-assertion in this connection. John Locke was much occupied by this phenomenon in its sociological relations. Locke



says that self-esteem is the satisfaction at being acknowledged by one's fellow man. Thus self-esteem makes the individual dependent on the views of the surroundings, and this again leads to resignation and suppression of the original inclinations. Similarly, Franz Oppenheimer emphasizes the "Trieb der gesellschaftlichen Hochgeltung" as the most important of all social impulses, the social impulse par excellence, whose satisfaction is the final goal of all social activity. Furthermore, Oppenheimer emphasizes that self-esteem is particularly active in the impulse to make a living, whose goal is not exactly possession, but reputation. This is naturally a somewhat crass formulation. But it seems beyond doubt that self-esteem and acknowledgment by others also play an exceedingly great part in the development of the need to make a living.

Turning to the type of man we are dealing with today, we shall find interesting phenomena in the impulse to make a living, particularly if we also include in our consideration an evaluation of the type of work. Beyond doubt this type of man offers special features which greatly influence their way of working, and which is of importance to the further forming of their social life.

They very often belong to the lonely type of workers; they like to get special tasks, where not too much cooperation is required. They have very often a pronounced sense of the formal, of the stringent, but are at the same time prosaic and often purely pedantic, with a marked sense of extreme standpoints. In addition, they very often have a pronounced power of abstraction, but are also often opinionated.

They prefer *multum* to *multa*. Therefore Kretschmer points out that mainly schizothymic and schizoid individuals go in for strictly systematic and philosophic research work. Furthermore, he points out that idealists, revolutionaries and reformers are often of a strikingly schizothymic or schizoid character. Here is free scope for their fanaticism and despotism. Schizoidiacs lack completely the amplexity of the cycloid—his realism, his need for what can be registered by the senses together with a tendency to empiricism and a leveling attitude. Yet we can often see that schizoidia may condition highly valuable positive social activities, although they do not allow of any compromise.

Of major interest from a social-psychiatric point of view, however, are the deviations in a more negative direction. Stagnation and regression phenomena may be facing us here, especially during the development of the schizophrenias.

Strikingly often we meet with the seeking and fumbling of the juvenile stage, marked by instability and deficient continuity. Typical of these individuals are restless and inexplicable wandering from one occupation to another, from school to school, etc., without any result.

Extinguished school lights, wrecked artistic talents, emigrants sent home, on the whole the "déclassés," belong most often to this category. In this connection we point to the demonstration by Oedegaard and others of the relatively high amount of schizophrenia and probably also schizoidia among emigrated persons, a relation which has been ascribed to their generally reduced social contact feeling. Dunham's ecological examinations of schizophrenia in Chicago show a distinctly skew distribution of frequency, so that the cases of schizophrenia accumulate in, socially speaking, the more disorganized parts of the town. On the other hand the manic-melancholiac cases show a more even distribution.

We also often find a peculiar inadequacy between the purely personal qualifications and the choice of occupation. In the usual social life they may fail completely, and yet no goal is too

high for them, such as dramatic poetry, philosophy, studies in religion, astronomy, etc. Such a development may often be traced back to late puberty, and then the picture often assumes the character of hebephrenia. But it is exceedingly interesting to notice that the same abnormal attitude of life may also take form at a later, maturer age after a previous normal development of the impulse to make a living, as we see a distinct break with the social curve of life. In addition, we often see mental dissociation phenomena, which, according to experience, usually accompany this sort of social decay. The desocialization and the schizophrenic decomposition of the personality are most often two aspects of the same case. But it is peculiar that we may also have to face such situations with an inexplicable social and professional decay without indication of intra-psycho ataxy. Often, but not always, schizothymic features in the premorbid personality of these patients may be demonstrated. These conditions are exceedingly interesting, but difficult to classify. Examples are: The well-to-do engineer, ending as a private boarder in the country, ruined, given to absurd poetry-making; the college candidate ending as a milkman; the veterinary student spending his whole fortune by traveling to various European countries and coming home with a full beard and his suitcase full of impossible manuscripts, etc.

This condition differs from all other forms of mental sufferings in so far as the social misrelation seems to come from an incomprehensible, primary abandonment of the social ambition. Considering their intellectual and moral equipment, and often also the sphere of sentiments, one would have expected them to think and act differently from what they do. They differ from the classical schizophrenia in so far as they do not, as mentioned above, offer any phenomena of dissociation.

On the other hand, they show several similarities to the classical schizophrenia. Thus they may show the same inner mental stereotyping and drying-up. Furthermore they may, like schizophrenics, offer a pronounced contempt of society and spirit of opposition, a relation in schizophrenias especially emphasized by Evensen. The previously mentioned family opposition is also usually very conspicuous. Both schizophrenics and socially decayed individuals, as we may call them, are in no need of the normal feeling of satisfaction, which is based on acknowledgment by other people. If they have a certain need of it, they try to acquire it by means which to them are impossible, and which only lead to total social failure. Connected with this is also the peculiar and completely incomprehensible, selfish feeling of satisfaction, which, despite the deepest decay, is characteristic of these conditions.

Whether we shall classify these conditions in the schizoid or schizophrenic group, is of less importance to us today. We simply state that, according to all probability, they must be reckoned in one of these classes.

And we must, as it seems, consider as probable that schizophrenics all in all have a primary, incomprehensible social defect, a displaced, reduced self-confidence, and that this is the primarily active factor in the process of desocialization also where the vocational aspect is concerned. There seem to be disturbances in the phenomenon that Toennies sets up as the will for social life.

Toennies holds that the social life of man is based on two kinds of wills; first, the natural emotional impulse which he calls the will of being, which forms the basis of the purely social relations, and second, the will of choice based on intellectual motives and self-interest, which

gives the impetus to society-formation. This is the same motive which forms the basis of Hobbes and of Rousseau's "Contrat social."

If we adopt Toennies's view of the problems, we may say that at the highest degree of de-socialization, namely, that which we see in schizophrenia in the form of autism, both the will of being and the will of choice have partly been abandoned. The schizoid persons may in general be said to be in the possession of a certain will of choice. They maintain on the whole the contact which is necessary to get work. As regards the separate socially decayed individuals mentioned above, those with seriously impaired vocational impulse, we must say that their will of choice has been impaired to the highest degree, partly almost abandoned, thus approaching the classical schizophrenic situation. Socially speaking, a high degree of intra-social ataxia has arisen in both cases.

We have tried here to adopt a view of integration of the social defects of schizophrenic conditions. Naturally, the surroundings will play a part. For, as we have already said, the socialization does not only depend merely on inner personal, but also on outer social factors. But the reduced power of sociability seems to be the primary factor in the development, which then can be led over into a *circulus vitiosus*, where disposition and surroundings mutually influence each other. This may be the case with all the sociological situations we have analyzed.

We want to emphasize the term "sociability," as it represents the dynamic factor in conformity with the term "integration." For we believe that since Bleuler and Kretschmer formed the terms schizophrenia and schizoidia, we have come to adopt too narrow views of these conditions, just as we are inclined to consider the social forms of expression of these conditions as pre-formed, fixed, unchangeable and irreversible. A more intense psychotherapeutic treatment of these conditions will show that this is not the case.

Of special interest in this connection are the almost puzzling results in the treatment of schizophrenia reported by Rosen. It is maintained that the most self-satisfied autism can be removed, at any rate temporarily. However, a considerable amount of hours of treatment per patient is required. Furthermore, we see an increased contact feeling during bodily diseases, unexpected visits, removal from asylum to asylum, etc. Therefore, we prefer to apply the term "reduced sociability" instead of the usual ones such as asocial, lack of contact feeling, not social, etc. The term "reduced sociability" opens up certain mental-hygienic and therapeutic perspectives.

All those who are dealing with psychiatric problems know how difficult it is to evaluate the symptoms which in our opinion characterize the group of diseases which we today call schizophrenias. We mention in this connection Langfeldt's demonstration of the many schizophreniform conditions. We believe, however, that extended social psychopathologic points of view and investigations will help to determine more precisely this group of disease. Considering our present therapeutic means it seems to us that the prognosis is bad only when distinct desocialization has occurred. For desocialization together with phenomena of dissociation indicates that the mental totality, the superior regulating principle of co-ordination, has been brought out of balance. Therefore, we cannot adopt any particularistic view as regards these sufferings. As Gruhle maintains, we must work with a basic formula which describes the whole schizophrenic structure. But, *nota bene*, in this basic formula the social-psychopathologic element must be

evaluated equally with the purely intra-psychic phenomena. But again the social-psychologic factor must be evaluated in relation to the total life-situation, its longitudinal section as well as its cross-section.

## RESUMEN

La forma fundamental que adopta cada tipo de actividad mental es un proceso continuado de un mutuo dar y recibir. Por lo tanto el psiquiatría debiera interesarse mucho más en las alteraciones de las relaciones mutuas entre los seres humanos.

Los estados esquizofrénicos son precisamente los procesos que nos permiten apreciar con mayor claridad el valor que tiene el pensamiento sociológico en psiquiatría.

La capacidad de relación social se desarrolla teniendo como base el impulso de contacto social y siguiendo un proceso de socialización, o sea de integración social.

Considerando las relaciones humanas en general, observamos en los individuos esquizofrénicos ciertos defectos en este proceso de integración. Por lo general existe un debilitamiento del impulso de contacto, es decir, una reducción de la necesidad de contacto social.

Se alteran las costumbres sociales más elementales, como el saludo, la gentileza y los modales, especialmente la inclinación al saludar, el apretón de manos, fraseología, compostura y mímica.

La reacción a situaciones sociales más complejas también resultan defectuosas con mucha frecuencia en estos pacientes. Muy característica e interesante es su síntesis sexual incompleta, el bajo porcentaje de matrimonios entre los pacientes varones esquizofrénicos, las uniones de tipo claramente patriarcal o matriarcal y la inexplicable oposición familiar. También hallamos desviaciones de lo normal en la forma más elevada de sentimientos de confraternidad, o sea en los sentimientos religiosos.

La necesidad de ganarse la vida (basada en un sentimiento de autoafirmación, fuerza de voluntad y conciencia de las responsabilidades sociales) con mucha frecuencia es inestable y carece de continuidad. Debe considerarse como probable que el paciente esquizofrénico tenga un incomprensible trastorno primario del impulso de tumescencia o contractación. Si aceptamos el punto de vista de Toennies sobre los problemas sociales se puede afirmar que estos pacientes tienen un defecto en los dos tipos de voluntad social. La ataxia intrasocial debe valorarse sobre la fórmula básica de la esquizofrenia, junto con los fenómenos puramente intrapsíquicos.

## RESUME

La forme fondamentale de toute espèce d'activité mentale est un processus continu d'échanges, on donne et on reçoit. La psychiatrie doit donc s'intéresser aux troubles survenant dans les relations mutuelles entre humains.

Les états schizophréniques constituent les conditions mêmes qui nous permettent de voir le plus clairement l'importance de la pensée sociologique en psychiatrie. L'aptitude à vivre en société se développe sur la base de l'impulsion de contact social par un processus de socialisation — une intégration sociale. Considérant les rapports humains en général, les sujets schizophréniques présentent un défaut de ce processus d'intégration sociale. Ils montrent habituellement un affaiblissement de l'impulsion de contact. Leur besoin de contact social est réduit. Les normes sociales les plus élémentaires, telles que l'abord, la politesse, la décence sont altérées. Ceci est particulièrement vrai du salut, de la poignée de main, de la phraséologie, de l'attitude, de la mimique.

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Nous trouvons aussi que, chez le schizophrénique, les situations d'ordre plus particulièrement social sont très souvent caractérisées par leur défaillance. Ceci est également particulier, et des plus intéressant, en ce qui concerne la synthèse sexuelle incomplète, le faible pourcentage d'hommes schizophrènes qui se marient, les alliances du type patriarcal et matriarcal caractérisé et l'opposition familiale incompréhensible. Dans la forme la plus élevée du sentiment de communauté, les sentiments religieux, il existe aussi des déviations de la normale.

Le besoin de gagner sa vie, qui est basé sur l'affirmation de soi-même, la volonté et la conscience de responsabilité sociale manquent très souvent de continuité et de stabilité chez le schizophrénique. Il semble que nous devrions considérer comme probable, l'éventualité chez l'individu schizophrénique d'un défaut primordial incompréhensible de l'impulsion d'affectivité. Les schizophréniques présentent des défauts dans deux formes des nécessités sociales. Dans la schizophrénie l'ataxie intra-sociale doit être évaluée à égalité avec les phénomènes purement intra-psychiques.

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# Suicide

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When Hamlet considered with himself a possible resolution of his intolerable situation, if "the Everlasting had not fixed His canon 'gainst self-slaughter," he was not quoting "the Everlasting" but rather the transitory, namely, St. Augustine and other spokesmen of the early Christian church who, in opposition to the tenets of the "pagan" religions that church was supplanting, created the dogma that suicide was a heinous sin.

For the antique world death not only ended the turmoil of life; to a life of suffering it was even a desirable end which might justifiably be self-achieved. But the new religion pictured death not as an ending but as a beginning, and for the ungodly a beginning of a rather unpleasant eternity. Successive councils of the church confirmed and emphasized the utter sinfulness of suicide. Said St. Chrysostom, "If it is base to destroy others, much more is it to destroy one's self" — a statement which seems to take logic by the throat. The *reductio ad absurdum* was reached in the dictum that Judas committed a greater sin in killing himself than in betraying his master.

Such were the ideas, however, which prevailed in pre-Renaissance times; they were accredited and accepted opinion. They passed into the mores of the people; they became clothed with the forms of law. Suicide henceforth was regarded as a double-barreled offense — against both church and state. It was at the same time a sin and a crime; although Schopenhauer reminds us that "neither in the Old nor in the New Testament is there to be found any prohibition or positive disapproval of it." He points out further that "it is quite obvious that there is nothing in the world to which every man has a more unassailable right than to his own life and person." Pliny long before had reflected that "life is not so desirable a thing as to be protracted at any cost. . . . Among the blessings which Nature gives to man, there is none greater than an opportune death; and the best of it is that every one can avail himself of it." And Seneca: "As I choose the ship in which I will sail, and the house I will inhabit, so I will choose the death by which I will leave life. . . . If life pleases you, live. If not, you have a right to return whence you came."

The Roman doctrine that death was the end of suffering and a law of nature — *Lex non poena mors* — was contradicted by clerical teaching that death was punishment for the sin of Adam; and church and state conspired to visit vengeance upon the suicide. His spirit was beyond their reach but his property they could confiscate and his body they could shamefully entreat.<sup>1</sup>

With the Renaissance the more humane ideas of Graeco-Roman culture concerning life and death were voiced again by some of the world's great thinkers, and from the seventeenth century onward suicidal acts have lost somewhat of the sinful, but less of their criminal, quality. Outside the Judeo-Christian and Mohammedan peoples there has never been the same hue and cry about self-inflicted death.

<sup>1</sup>Not until 1870 were forfeitures of the lands or chattels of suicides abolished in Great Britain. Burial at four cross-roads with a stake driven through the body was abolished by statute in 1823.



And how stand matters today in our western civilization? The shadow of sin still dimly lingers, owing to a traditional obligation to deity which the suicidal act repudiates.

From the standpoint of British law the act is still a crime — *felo-de-se* — whether or not the rights of others are thereby infringed, and attempted suicide is punishable by imprisonment. This is true also in Canada, where criminal procedure differs from that in the United States in that the Federal Criminal Code applies uniformly throughout the Dominion. Section 270 of the Criminal Code of Canada reads: "Every one who attempts to commit suicide is guilty of an indictable offense and liable to two years' imprisonment." In the United States, I believe, there are not more than four states in which a suicidal attempt is still regarded as a criminal act.

A third viewpoint somewhat popular in contemporary usage is that a suicidal act is evidence of mental derangement. This is the common fallacy of generalization, and the assumption can be supported neither by experience nor by statistics. The fact that the impulse to self-destruction is a conspicuous symptom in certain mental diseases is no warrant for concluding that all persons attempting to or taking their own lives are insane. The weakness of the argument is manifest in the extraordinary verdict so frequently returned—"suicide while temporarily insane." This verdict may be rendered even though up to the time of his death the mental health of the deceased was never in question, and when the only possible "evidence" of derangement is the act of suicide itself. This of course is an entirely conjectural assumption that can be neither proved nor disproved. Does it not suggest, however, that the morbid psychology involved refers not so much to the subject of the inquest as to the social attitude which demands or approves such a verdict?

The question is whether one arbitrarily takes the position that a suicidal act is in itself and without other evidence a symptom of mental derangement. So distinguished an authority as Sir Hubert Bond espoused the traditional view. Commenting on the well-known relationship of suicide to mental disorder, he states: "My belief is so firm as to amount to a strong doubt as to the existence of sane suicides."<sup>2</sup> The insecurity of this position becomes evident in Sir Hubert's continuing remarks: "I feel sure that the more closely individual cases are studied the more it will be realized how difficult, if not impossible, it is to be sure at the time of the act, even if only an attempt, that the doer was not mentally disordered." Quite so; but certainly no less difficult or impossible to be sure that the doer *was* mentally disordered. Moreover, the verdict of "temporary insanity" in these cases is brought in by process of law; but the law holds every man sane until the contrary is proved. The situation involves a curious medicolegal paradox; and it would be hardly logical for the medical expert to lend his authority to the judgment that a thing is so, merely because it cannot be proved that it is not so.

The popular and uncritical tendency to accept the suicidal act as evidence of insanity is reflected in the fact that from inquests held on 4,846 suicides in England and Wales in the year 1928, the verdict of *felo-de-se* was returned in only 88 cases. Contrasting with these figures is the statement of W. Norwood East, Commissioner of Prisons, that of some 3,000 cases of attempted suicide examined by him, only about one-fifth could be regarded as certifiable. The *British Medical Journal*,<sup>3</sup> commenting editorially on the Eastbourne symposium, points out that

<sup>2</sup>Symposium on suicide at the annual meeting of the British Medical Association, Eastbourne, 1931.

<sup>3</sup>August 8, 1931.

among approximately 5,000 successful suicides reported annually in England and Wales,<sup>4</sup> an average of only about 50 occur in the certified insane. The British Medical Journal continues: "The vast majority of the suicides are not in any ordinary sense of the word insane, *pace* Sir Hubert Bond—unless the act of suicide itself defines insanity, which by the present law, as Dr. East showed in his paper, it clearly does not."

The disingenuousness of the public attitude—and of the legal and medical as well—with regard to the suicide question is revealed in another medicolegal paradox, namely, that in general the verdict "sane" or "insane" hangs upon the question whether the individual fails or succeeds in taking his life. If he succeeds he is declared insane and thereby absolved from all blame; if he fails he is held accountable for his act and in the jurisdictions where a suicidal attempt is still regarded as a crime is liable to prosecution. It is as if one and the same man at one and the same instant of time were either sane or insane according to the issue of his act.

But most curious of all is the willingness with which friends of the suicide accept the judgment that he was mentally deranged, although under all other circumstances they would resist such a suggestion to the uttermost. The "stigma" of insanity seems to be preferable to the painful perplexity, humiliation, perhaps even a sense of guilt, in admitting that a member of one's own family could choose to kill himself if in his right mind.

Not so many years ago a world figure, a great and good man, ended his own life. When George Eastman, the inventor of the Kodak, dismissed his friends from the room, wrote his final message, and fired the fatal shot, there was nothing in the circumstances to distinguish his conduct, so far as his state of mind and reasoned purpose are concerned, from any other planned action in the ordinary affairs of life. The facts of Mr. Eastman's life were so well known, his mind and character were of such fine quality, and his value to the world has been so great, that his last courageous act is beyond cavil.

From many authorities, we must limit quotation to two additional British opinions. Said Hack Tuke: "It cannot be admitted for a moment that the suicidal act taken alone is any sign of insanity." And Henry Maudsley: "Just as madness may exist without any idea of suicide, so suicide may take place, the effect of a full and free determination, formed by a healthy mind, and executed with the coolness and complete system of precautions of the most perfect logic."

Possibly the most sensible coroner's jury verdict on record was rendered following the suicide of the Adjutant General of Mississippi, who shot himself in his office in the National Guard Armory at Jackson in 1932. The jury found that the deceased came to his death by his own hand "for reasons best known to himself."

We may look upon the act of self-destruction as a universal phenomenon in the sense that it occurs in mentally sound persons as well as those of unsound mind. Unquestionably the idea of suicide enters the minds of vast numbers of persons at one time or another, although quite unsuspected by others and seldom resulting in an overt act. When actual mental disease is present, the risk of suicide, in varying degree, exists in almost every form of the disorder, but

<sup>4</sup>The B.M.J. quoting statistics for England and Wales reports 5,263 suicides in 1938. There was the customary decrease during wartime, with 3,651 cases in 1944. In 1945 the number had risen to 3,818.

is of course greatest in depressive states or associated with depressive trends, whatever the diagnosis and whether in early, midlife, or involutional years.

In this connection there is one point to be especially emphasized: the diagnosis of neurasthenia or of a neurosis is no guarantee that a serious or fatal suicidal act will not occur. Although there is evidence enough to bear out this statement, there has been a rather widely credited assumption, supported by medical authority too, that a patient who is merely "nervous," perhaps under private care at home, is not a suicidal risk. Depression is depression whether we call it neurasthenic or reactive or involutional or manic-depressive; and an attempt to differentiate a benign from a more serious mental state on the basis of an arbitrary psychiatric diagnosis is to incur an entirely unwarranted hazard.

Incidentally, psychiatric diagnoses have appreciably lost caste within recent years. They are not the clear-cut, mutually exclusive pictures some of us of the older generation used to believe in. There are too many atypical forms, too many transitional forms, too many mixed forms; and at length we realize that they are all *individual* forms. Instead, therefore, of basing prognosis—and that includes the danger of suicide—on a hypothetical diagnosis, one seeks to know the trends, motivation, and suicide potential of the individual patient. It then becomes apparent that anyone who is melancholy, who morbidly devaluates himself or is burdened with a sense of guilt or shame, who is the victim of painful fears, who feels himself helpless or useless or a burden to others, who believes that he is regarded with dislike by those about him or expects harm from known or unknown agencies, anyone whose picture of life present and future has no pleasant feature, who feels hopeless of again being active and happy, or one who is suffering from sheer *ennui*—any such may in the end attempt self-destruction.

But just as there are various forms of mental illness, so there are different types of suicidal act from the standpoint of motivation and of prognosis, and of management and treatment. Disregarding, therefore, the possible psychiatric diagnoses, it may be helpful to focus attention on the suicidal gesture itself as expressive of a state of mind and to review the commoner varieties.

First, and more important than all others together from the standpoints of suffering of the patient and difficulty of successful management, is the type that may properly be called *malignant*, such as occurs in the severer melancholics that require safeguarding and treatment in a psychiatric hospital. Such a patient may have been a serious hazard for long months before he is brought to hospital. Even after the hazard is recognized, an overt suicidal act may be required to move those concerned to action. We read now and then in the newspapers of a depressed patient who for a prolonged period has been under private psychiatric care and who has unexpectedly jumped from an upper window or taken an overdose of sleeping tablets surreptitiously accumulated.

What are the characteristics by which a typical severe example of this variety of suicidal motivation may be recognized and its risk estimated? Ideas of self-destruction have probably tormented the patient for a long time, gradually growing more insistent until at length they appear as the only outcome of an intolerable situation. Some fortuitous event or imagined threat may then cause these ideas to flare up, dominate consciousness, and rush the victim on to the tragic climax.

In the malignant suicidal type if the first attempt does not succeed, another may be expected almost surely to follow, and another and another until the patient either accomplishes his purpose or recovers. It is also characteristic for the sick person to express deep disappointment if his attempt is frustrated and to blame those who have been instrumental in keeping him alive. This attitude contrasts with that to be mentioned a little later in connection with another type.

In the mind of the malignantly suicidal patient there is an almost incredible concentration upon the single purpose, excluding every other consideration—a sort of gun-barrel mental vision. The formerly devoted husband or wife or parent, the business or professional man who has conscientiously fulfilled all his obligations as a good citizen and has observed the customary social, legal, and religious sanctions now becomes totally oblivious of all these relationships and of what are normally the most elementary duties. These matters are simply not in the patient's consciousness. What, for example, is to become of his family is not a problem for him to deal with because it does not present itself to his mind, or if it does it is as if it were no concern of his in the presence of the one overwhelming impulse, the fixity, exclusiveness, and urgency of which is something that cannot be experienced and can hardly be appreciated by the normal mind. Recovered patients have tried to describe this state which to them also in retrospect seems scarcely to have been possible.

Constant supervision in the care of such a patient self-evidently means every second of every minute of every hour in the twenty-four. Even then the issue becomes a kind of contest in which patient and nursing personnel are matching wits. That the odds in many cases are against those charged with the safety of the patient is understandable. Beside the everpresent element of human fallibility there is the vast discrepancy in the absorption of mind—the preoccupation—on the two sides. The contest is between a mind with just one thought and purpose morbidly intensified and that of the nurse, which like any mind in health may find it difficult to focus so intently and continuously through every moment of her tour of duty and without distraction on the single objective of uninterrupted supervision. If there is a momentary lapse of attention it is less likely to be on the part of the patient. In one case the patient asked the nurse to bring a glass of water from the adjoining bathroom. "Please let it run cold," he said. While the water was running cold, whatever time that may have been, he strangled himself with a suspender strap fixed to the bedpost by simply rolling out of bed. You ask how it could happen. Well, it happened.

Pathognomonic of malignant suicidal motivation are, in summary, (1) an affect state of severe dejection, (2) premeditation which may extend over a considerable period, (3) deliberate planning and choosing of opportunity, (4) concealment of motive, often with devices to mislead, (5) a single fixed purpose that blots out all contrary impulses, (6) disappointment and censure of rescuers if an attempt is frustrated, (7) repeated suicidal acts until the patient either kills himself or recovers.

Quite different from the malignant form is the *impulsive* variety. A good example is the sudden act of self-injury associated with an emotional storm in a person who may not have presented any definite signs of mental disturbance. Such an act may follow a lovers' quarrel or a domestic row, or any predicament in which the individual feels himself grievously wronged

or disadvantaged, needs sympathy or revenge, and under the emotional stress is not sufficiently stable to deal rationally with the situation.

A gesture of this kind, which is reactive to more or less immediate circumstances, is less likely to be fatal than in the former type. There is no premeditation or special planning or care for concealment. The shock of the act serves to relieve the emotional tension and after he is restored the patient is glad to find himself alive and is grateful to his preservers. Continuing symptoms of depression are not conspicuous. Cooperation, often in full measure, may be expected from the patient, and psychotherapy offers promise. In the average case the likelihood of repeated attempts is small, barring severe provocation, and constant supervision beyond a very brief period will not be indicated. A satisfactory psychiatric appraisal should be possible in a matter of days, and hospitalization greatly prolonged beyond the time required for dealing with the physical effects of the suicidal act will not as a rule be necessary.

A special instance of the impulsive or reactive type is that of the alcoholic patient in the phase of misery and self-depreciation following a heavy drinking bout. In such a case the suicidal act may be genuinely serious; but with convalescence from the debauch the suicidal impulse loses its strength.

It goes without saying that in no case of an impulsive act of self-injury should the patient be released from a hospital until a psychiatric appraisal has been made *and recorded* of possible risk involved.

→ A third variety may be called the *compulsive* type. Here there is less, or perhaps none, of the conscious voluntary element. The patient is driven to the act. It may be that accusing voices tell him he is not fit to live and bid him kill himself. Such symptoms may be suggestive of a schizophrenic process and one would look for other schizoid features. In a given case the question may be whether the phenomenon can properly be called an auditory hallucination or the voice of conscience with a sense of guilt, for we are told that conscience is "a still small voice." In this case the delusional motivation of the suicidal act would have to be considered, thus bringing the patient nearer to the depressive group as in our first category. While we have applied the term "malignant" to that first group, we realize of course that there are all degrees of depression and that the malignancy of the suicidal urge will vary accordingly. It is safer, however, to overestimate the danger than to underestimate it.

These three are the commoner kinds of suicidal motivation that the clinician will meet with. A number of others, however, are of interest. One may be described as suicide by *suggestion*. You may remember a Hungarian song of a dozen or so years ago in which both words and music were particularly mournful. It was called "Gloomy Sunday," and is reported to have been responsible for at least 18 suicides in Budapest. The police decided that the music must be suppressed when a letter was received from the 18th victim requesting them to place on his grave the 100 roses mentioned in the song. Some of these persons killed themselves while the piece was being played on their phonographs. We are reminded of the suicide epidemic that followed the publication of Goethe's "Sorrows of Werther."

The eminent 19th century British psychiatrist, Forbes Winslow, reports an instance of suggested suicide attributable to the philosopher Hume. Hume had loaned his famous essay in defense of suicide to a friend who, after reading it, shot himself. Winslow was a conventionally



religious man, and his attitude toward the somewhat unorthodox philosopher was not conspicuous in Christian charity; for in his own book, "The Anatomy of Suicide," he speaks of "the detestable author of this abominable treatise" and declares that on learning of his friend's fate Hume should have "terminated his own pernicious existence by a cord." And he added, "The cold-blooded infidel was too cowardly to execute summary justice on himself." Fortunately for the Scotch philosopher's peace of mind he had died 64 years before the Winslovian fulmination.

Several years ago a Japanese girl student from Tokyo climbed a volcanic mountain on a barren island just off shore and plunged into the fiery crater. That started the parade. During the next two years others followed at the rate of three a week, and a vastly greater number were frustrated in the attempt. A lively tourist traffic had got under way and not infrequently at first visitors to the rim of the crater would be repaid by witnessing a suicidal leap. The thrifty Japanese took advantage of the popularity of the island and converted it into a pleasure resort. They built hotels, provided riding horses and taxi service to the crater; also gravity railway cars down the side of the mountain for those who felt disposed to return.

In families where one or more suicides have occurred other members are sometimes moved to kill themselves by a sort of *autosuggestion*, especially when they reach the age at which the other deaths took place. As they tell their story it seems to them almost as if they were under a family curse, or impelled by a malign fate as in a Greek tragedy, from which they could not escape. They may express the belief that the suicidal impulse itself is hereditary. There have been fairly numerous instances of this familial tendency, usually associated with mental illness in one or another member who may have set the example. In one family reported a few years ago there were eight suicides in three generations. Two of these were depressive patients, but five were never considered to be psychiatric cases. Possibly the family suicide record is held by the Briggs family of Connecticut, in which twenty-three suicides occurred among four generations over a period of fifty years. It is particularly in the so-called suicide families that psychotherapy should be of value as a prophylactic, in counteracting the autosuggestion factor.

Many of the suicides by suggestion or autosuggestion are cases of imitation. In a kindred form the motive may be called *fascination*. Many persons in health have experienced this potentially dangerous impulse of fascination for self-destruction. Who has not felt the urge to plunge from a high bridge or from the observation platform of a tall building or from the edge of a precipice? Such a state of consciousness represents the ambivalency that underlies so much voluntary motor activity. Or call it a variety of phobia if you like. A friend of mine would not trust himself near an open window on an upper floor of a skyscraper. Standing on a railway platform have you never imagined yourself leaping in front of the oncoming engine? These almost universal experiences if exaggerated may become seriously disabling phobias; and suicides have occurred after all these fashions without more evidence as to motivation than the sudden yielding to an irresistible or unresisted impulse born of the fascination of supreme danger. There are men who dare not shave themselves with an open-blade razor for fear of impulsively cutting their own throats. Lord Byron expressed the belief that no man ever took a razor into his hand without thinking how easily he could use it in a suicidal act.

Fairly frequent, of course, are gestures that appear to be suicidal but are not so intended—self-inflicted wounds as means to an end other than death, to gain attention or sympathy or



advantage. Occasionally a *spurious* attempt of this sort may accidentally be carried too far.

An accident was reported some time ago in England that looked very much like a genuine suicidal act. A mental patient not under strict surveillance was found lying on the ground under an open window in an upper story. He was able to explain that he had been communing with the Deity and that when he heard the voice of God saying, "My son, come and seat thyself by my side," he had opened the window and stepped out to obey the divine command. He had expected to go up instead of down.

Suicides of *adventure* have been recorded, as revealed in antemortem notes in which the deceased has expressed curiosity about the sensations of dying or the conditions of an after-life. Such records may have to be taken with a few grains of salt, although there are undoubtedly morbid states in which preoccupation with death and after-death acquires a strong fascination.

Another unusual type is the *anbedonic* suicide. There is an occasional individual of temperament so phlegmatic that all the urges of normal living are of greatly reduced intensity. He is victim of a kind of involuntary asceticism. His appetites are weak and his satisfactions likewise. For him there is no warmth in social relationships, and at length between living and dying there seems to be little choice. Finally in the sheer boredom of existence, by a casual, almost impersonal act he terminates his life.

Persons of this quality have expressed themselves quite clearly and apparently sincerely. They are able to carry on with the daily round; they are not in need; no one is trying to make life difficult for them. Life is just not interesting. There is no zest in work and no pleasure in play. When they give up life it seems to be not so much that existence is painful as that it has no value. To this sort of personality Hume's unfortunate statement might apply when he declared his belief "that no man ever threw away life while it was worth keeping."

Most pitiful of all are the *juvenile* suicides—children who at the season we like to think of as the happiest have already found only defeat and misery. A little boy takes his life because his father is in jail and his mother is a drunkard and he cannot meet the taunts of his fellows. For one little girl who had been made a common drudge in the home, who had no pleasures and little even of comfort, life had ceased to be worth living. Unusual physical development also drives children to suicide. A lad of 16 and height 6 feet, 4 inches couldn't stand the teasing of boys of more normal levels. A girl of the same age was a teasing victim because of her 190 pounds weight. Many juvenile suicides are the result of school difficulties, inability to keep up with classes or to obtain high marks. One youngster left a note saying that he had killed himself because he "got a C in arithmetic." Fear of censure or punishment by unsympathetic parents for failing to pass an examination has led numerous school boys and girls to take their own lives. In addition to the downright cruelty of parents who have forgotten that they, too, once were children, the sheer insensitiveness of adults to the sensitivity of children with all its untoward consequences is one of the tragedies of our social life. Certain children have unfairly been called illegitimate. There are too many illegitimate parents, married and unmarried.

The psychopathology of suicide we have considered in connection with the various types of motivation that lead to the act. Certain generalizing theories have appeared in the literature, some of them fantastic, which need not detain us. Each case is a case by itself and must be so studied and dealt with. And in such study we do well to observe the Law of Parsimony, avoiding

complicated, involved, or far-fetched explanations when simpler ones suffice, based on elementary psychological principles, common sense and common knowledge of human reactions.

One general principle enunciated by the French sociologist Durkheim may be accepted as well established, namely, that "suicide varies in inverse ratio to the degree of integration of the social group, whether on a religious, family, or national basis." The reasons for this law are obvious. In a closely knit society all members share a common sense of security which is much weaker in a loosely organized society where individuation is a more prominent feature.

However, while in our western culture men differ widely in their attitude toward life and death and in their preoccupation with temporal problems of past, present, and future, nevertheless the average healthy-minded person lives for the most part in the present tense—as Osler put it, in day-tight compartments—without undue worry over past mistakes or borrowing the possible troubles of future days or years. And just as, because of clouds, sunlight may not visit the landscape evenly, so in daily living, both in health and illness, there may be stronger lights and shadows. And just as happy circumstances make us cling to life, so the burden of sorrow and suffering may lead on to thoughts of death. Since death, thus far, is a law of nature, we think of it as the established termination, according to protocol, both of the life span and the life work. "My work is done," wrote George Eastman in his brief note to his friends before firing the shot through his heart. He was 77 years old and his mind was clear. But for another whose mind is clouded by illness or so distraught from whatever cause that the prospect seems hopeless or intolerable, what more natural than the conclusion that life is virtually ended and should therefore be made so in fact?

The pity is that this conclusion may be a pathological one and that if not safeguarded and treated a useful life may be lost. It is the province of the physician and the nurse, public health personnel, social workers, clinical psychologists, welfare workers, all who come in contact with patients in general hospitals, psychiatric hospitals, outpatient clinics or private practice and in the community to be alert to warning signals<sup>5</sup> of suicidal risk. The fact that a person has not attempted suicide or has not spoken of it gives no assurance that he has not thought of it or is not contemplating it. There has always to be a first time.

The law may take no cognizance of a criminal until an overt criminal act has been committed, although the *mens rea* may have been present a long time; but in medicine, dealing with a sick mind, it may be gross neglect to wait for the act of suicide when the morbid intent and hazard might have been appreciated and measures of safety taken if more thorough investigation had been made.

The treatment of the patient with suicidal thoughts or intention, or who has made an attempt to kill himself, is of course the treatment of the underlying mental condition. This includes as perfect means of safeguarding as humanly possible and specific attention also to eventual social factors, domestic, occupational, or economic. With a patient who has any degree of insight, or who is capable of even the slightest cooperation, psychotherapy may play a very significant role, and its conscientious use with such a patient, having due regard to the peculiarly individual features of each one, will be rewarded by the preservation of many a life that is worth living.

<sup>5</sup>Some indications of suicidal risk are:

1. Severe depression with self-depreciation and self-blame.

2. Excessive worry over physical health.
3. Excessive worry over sleeplessness.
4. Fear of losing one's mind.
5. Fear of losing self-control and doing damage or injuring others.
6. Fear of punishment, torture, surgical operation.
7. States of inaccessible agitated depression.
8. Dread of being a burden to others.
9. Dread of discharge from the security of the hospital. In one case, the doctor made the note after his visit, "Patient improved but won't admit it." Suicide two days later.
10. Persistent tendency to seek seclusion.
11. The discouragement that goes with depressive exacerbations during convalescence.
12. Abrupt apparent improvement with relaxed vigilance by nursing personnel.
13. Promises by a depressed patient with request for greater liberty or privacy.
14. History of previous suicidal attempt.
15. Family history of suicide, especially a recent case or at same age as the patient.
16. Recent suicide of an intimate friend.
17. Future living conditions actually unfavorable, without prospect of happiness or security.
18. Death wish and talk from whatever motive.
19. Anhedonic personality factors.
20. Patient's reaction to either unnecessarily irksome and rigid or too lax supervision and safeguarding.
21. Time of year and day—more suicides occur during spring and early summer. Hospitalized patients often choose the early morning hours, especially at the time when night and day nurses are changing.

#### RESUMEN

En este trabajo se consideran varios puntos de vista pasados y presentes referentes al suicidio: 1) como el acto voluntario de una mente normal; 2) como un acto pecaminoso; 3) como un acto criminal; 4) y por último, como síntoma de una enfermedad mental. Se estudia la influencia de la doctrina cristiana en relación con las citadas opiniones. Existen numerosas pruebas demostrativas de que el acto del suicidio no es un signo inequívoco de un trastorno mental. Las tentativas de suicidio pueden ocurrir en cualquier forma de enfermedad mental caracterizada por un estado de depresión emocional, siendo factores más importantes establecer el tipo y grado de la misma que un diagnóstico psiquiátrico definido. El autor no comparte la opinión de que los pacientes clasificados de psiconeuróticos no estén expuestos al suicidio. Se examinan los distintos tipos de motivos de suicidio y el grado de peligro que entrañan, descartando el diagnóstico psiquiátrico. Se describen los signos y síntomas más importantes mediante los cuales se puede reconocer el riesgo de suicidio, y se indican las medidas de precaución y el tratamiento.

#### RESUME

Le présent article traite des divers points de vue actuels et passés au sujet du suicide: (1) comme acte volontaire d'un esprit normal, (2) comme acte coupable, (3) comme acte criminel, (4) comme symptôme d'une maladie mentale. L'influence de la doctrine chrétienne est mentionnée dans l'élaboration de ces points de vue. Les preuves abondent qu'un acte de suicide n'est pas en lui-même l'indication certaine d'une maladie mentale. Des actes de suicide peuvent survenir dans n'importe quel cas de maladie mentale caractérisée par un abattement émotionnel, et le point important est le type et le degré de l'abattement mental plutôt qu'un diagnostic psychiatrique catégorique. Le point de vue que les sujets classés comme psychoneurotiques ne présentent pas de risque de suicide ne peut se soutenir. On indique aussi les indices et symptômes importants qui permettent de reconnaître le danger de suicide, ainsi que les mesures de précaution et de traitement qu'il convient d'adopter.

# Significance of the Thalamus in Psychoses

## WITH REFERENCE TO HALLUCINATIONS AND DELUSIONS

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Consciousness, perception and experience are rightly regarded as functions of the cerebral cortex. If we add to these the processes and patterns of motivation which make learned behavior possible, the functions of the cortex assume the role of an adjusting and goal-directing mechanism capable of using past experience as the discretion of each moment suggests. This is overt behavior using the bodily muscles and visceral resources as the effector agencies in the body and limbs. Speech, prehension and locomotion are the channels of expression of learned behavior. There is, in addition, a certain internal counterpart of speech, locomotion and visceral life which expresses itself in silent contemplations, thought and imagery not necessarily accompanied by overt behavior. In this age of schooling much effort is devoted to the development of this silent, inarticulate inner life and thought processes. This is regarded as a preparation for adjusting, acting and living in a complex modern society which requires grace, knowledge and skills of many kinds directed toward socially approved activities. For all this directed activity, leading from the past into the present, the cerebral cortex is the master organ.

The cortex, however, is only the luminous screen upon which all experience from the outer world is projected and retained in a kaleidoscopic way. Habits, the residual of past experience, symbols, the elements of temporal sequences, needs and motives have a definite representation in this projection sphere. Each element of cortical activity has a pattern of its own which recurs with fidelity. How these patterns are produced and how they attain a remarkable fidelity in the cortex of the brain, has been the quest of many generations of philosophers, psychologists and material scientists. In recent years it has become evident that the functions of the cerebral cortex can be referred to cerebral mechanisms, so organized as to make the reception of patterns of sensory and internal experience possible in a transcortical medium. By what means is this accomplished and what are the ways by which experience is bound to reality? These are questions which now can be answered in a tentative way. It seems appropriate to state that recent investigations leave little doubt that the thalamus is the complex subcortical organ which delivers all different projected experiences into the cortex and also participates in the orderly propagation of reflected processes of the silent inner life of the individual.

Every individual is bound to realities of the world about him by his sense organs and the sensory paths of nerve fibers which connect these organs with the cerebral cortex. All these paths pass to the thalamus where special cell masses act as relays for projecting these paths to sensory areas of the cortex.<sup>1</sup> Sensory radiations emanate from the relays of the thalamus and terminate in sensory areas of the cortex. This principle applies to all sense departments excepting smell, which has a separate system of direct cortical connections of its own. The dorsal thalamus may be defined as a group of nerve cell masses, about fourteen in number, which connect all the important different systems to the cerebral cortex. It provides for a local cortical as well as for an orderly transcortical distribution of nerve fibers and impulses to all areas of the cortex. The

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cortex is a surface organ not independent of the thalamus because it depends on the thalamus for contact with the outside world and the inner organs of the body, including subcortical levels of the central nervous system. Together the thalamus and the cortex constitute the essential machinery which turns out the mental process. Without the thalamus these processes could not be constructed on experiences derived from bodily sources and the external world.

In the posterior portion of the thalamus, there are five cell masses, represented in Fig. 1, which act as relays for a number of sensory systems.<sup>2</sup> The lateral geniculate body (lg) sends the visual radiations (vr) to the visual area in the occipital cortex. (Figs. 1 and 2). Patterns of visual impulses aroused in the cones and rods of the retina are gathered by the bipolar cells and ganglion cells of the retina, and are transmitted by the nerve fibers of the optic nerves and tract to the lateral geniculate body. The nerve cells of this body transmit these impulses by the visual radiations to the cells of the occipital cortex. The conduction characteristics of these nerve impulses are probably as specific as the stimulus itself, and their distribution has been shown to be a point for point projection of the retina on the visual cortex. If we assume as true the two foregoing statements, it becomes apparent that vision as experienced goes as far outward as the external reality itself. The total patterns of the objects or situations seen are recreated in the cortex in the original form and energy pattern. This doctrine has a broader significance since it can be applied to all the other sensory systems leading to the brain. The fact that cortical experience is projected to the body and to the outside world need cause no surprise. We can accept projicience as a property of all sense departments.<sup>3</sup> Its pathways are through the thalamus.

A histological examination of the cells of the lateral geniculate in psychoses, showed that they were invariably affected by disease characterized by inclusion bodies in the cytoplasm, destruction of cytoplasm and changes in the nuclei of the cells. Large sacs of inclusion bodies with intact cell contours were found in twelve cases of the paranoid type of dementia praecox (Fig. 4a). The distortion of cells and damage to their interior was extensive enough to account for a disturbance of conduction to the visual cortex and the production of abnormal visual phenomena. When the cells were partially destroyed, visual hallucinations were recorded in the clinical history. When the cells were largely destroyed, visual phenomena were largely absent, a condition common in passive, unreacting, deteriorated patients. We have found this cell loss in fifteen cases of senile psychosis with simple deterioration (Fig. 5h, i), with arteriosclerosis, metabolic disease, etc.

Sound waves, whose vibrations fall upon the hair cells in the inner ear, evoke nerve impulses which pass by auditory paths to the medial geniculate body (mg.) of the thalamus and are relayed to the auditory cortex in the superior temporal gyrus (Figs. 1 and 2 mg. r, aud.). Each sound is a burst of vibration frequencies, and sounds such as words follow one another in an orderly sequence. This temporal sequence of different words is necessary for the production of meaning at the cortical level.<sup>4</sup>

The nerve cells of the medial geniculate body showed a more severe incidence of disease and destruction than did those of the lateral geniculate. In paranoid psychoses, the cell population (Fig. 4b) was not as severely reduced as in the senile psychoses. Auditory hallucinations were prominent, and the amount of cell disease and destruction seemed to bear a relation to the char-

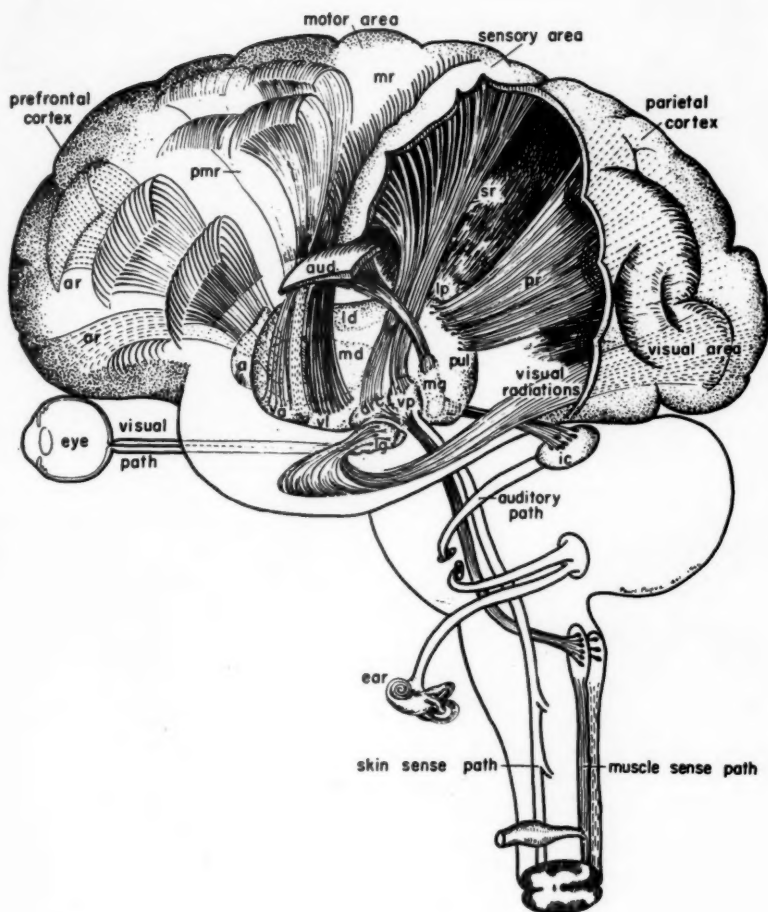


FIG. 1. Afferent paths, thalamic nuclei and radiations to the cortex. The visual path from the retina consists of the optic nerve and tract to the lateral geniculate body, lg, which sends the visual radiations to the visual area in the occipital pole. The auditory path from the ear passes to the inferior colliculus, ic, thence to the medial geniculate body, mg, which sends auditory radiations and impulses to the auditory area and in the superior temporal cortex. The paths from the sense organs in the skin, muscles and joints enter the ventral posterior nuclei, vp, arc, which send the sensory radiations, sr, to the cortex of the postcentral gyrus. The pulvinar, pul, has two way connections by the sensory radiations, sr, with the parietal association cortex. The medial dorsal nucleus, md, receives transthalamic fibers from the pulvinar and other nuclei and sends the orbital radiation, or, to the orbital cortex, and the anterior radiation, ar, to the prefrontal cortex on each side of the middle frontal gyrus. The ventral lateral nucleus, vl, receives the brachium conjunctivum and sends its radiations, mr, to the motor cortex in the precentral gyrus. The ventral anterior nucleus, va, receives fibers from the inner division of the pallidum and sends its radiations, pmr, to the premotor cortex. Connections of several other thalamic nuclei are not represented.



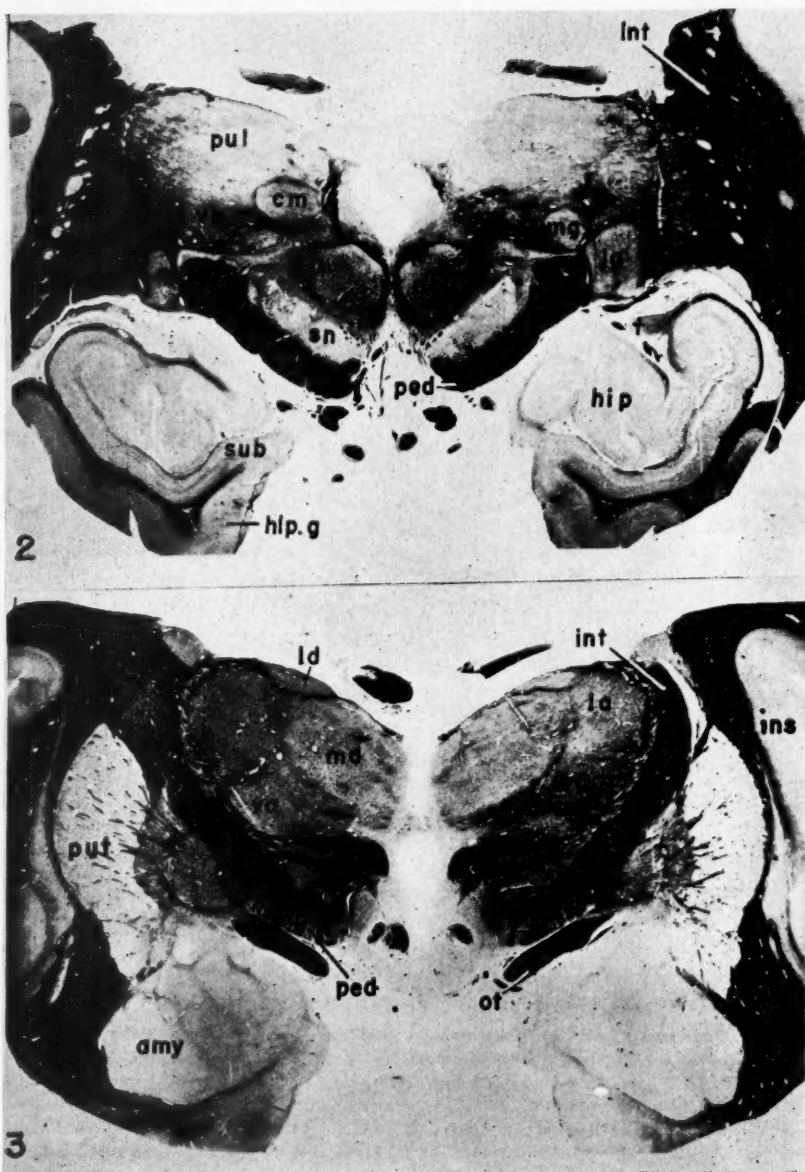


FIG. 2. Section through posterior part of the thalamus showing position of thalamic nuclei. Weigert stain X 3.

FIG. 3. Section through middle of the thalamus showing position of thalamic nuclei; amy, amygdala; am, centrum medianum; hip, hippocampus; hip. g, hippocampal gyrus; ins, insular cortex; int, internal capsule; la, lateral anterior nucleus; ld, lateral dorsal nucleus; lg, lateral geniculate body; md, medial dorsal nucleus; mg, medial geniculate nucleus; nr, red nucleus; ot, optic tract; ped, cerebral peduncle; pul, pulvinar; put, putamen; r, auditory radiations; sn, substantia nigra; sub, subiculum.

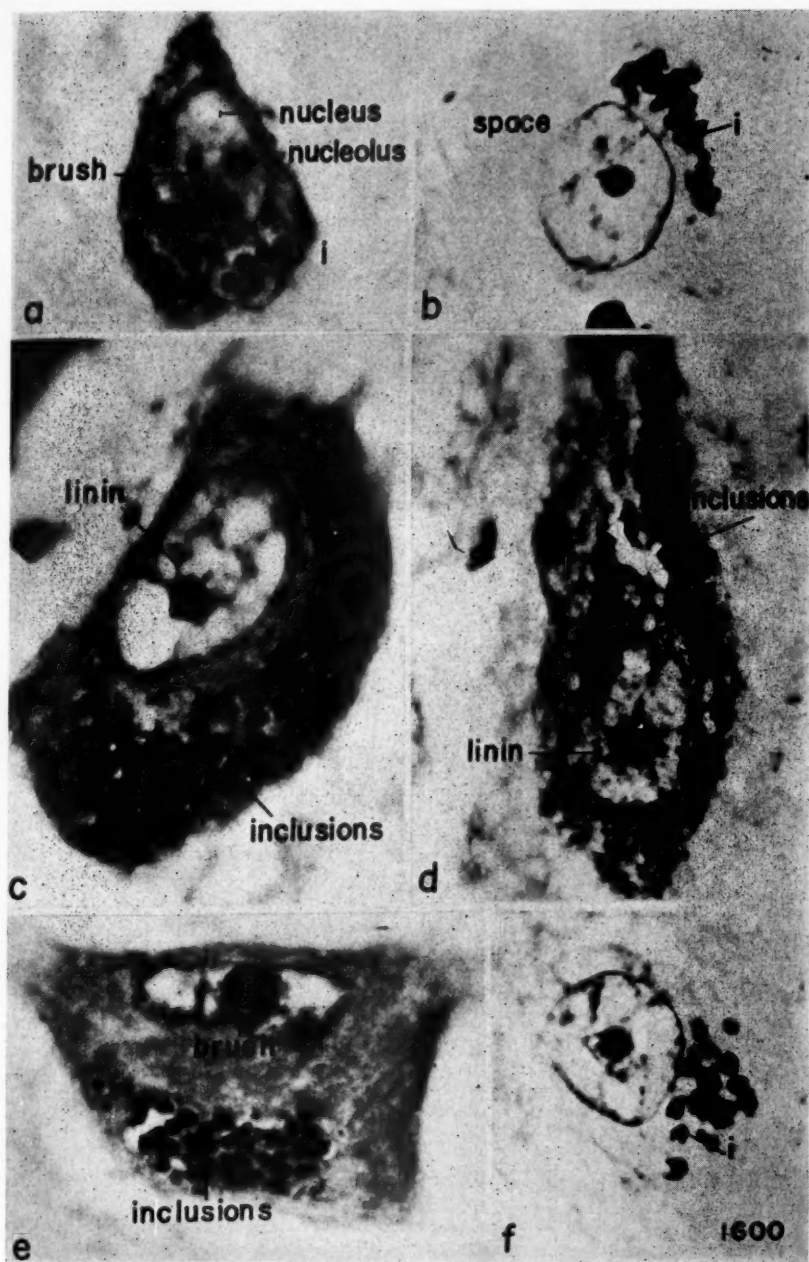


FIG. 4. Single nerve cells from different thalamic nuclei from paranoid types of psychoses, X1600. a, cell from lateral geniculate body; b, cell from medial geniculate body; c, cell from ventral posterior nucleus; d, cell from hippocampus; e, cell from ventral lateral (intermediate) nucleus; f, cell from pulvinar.

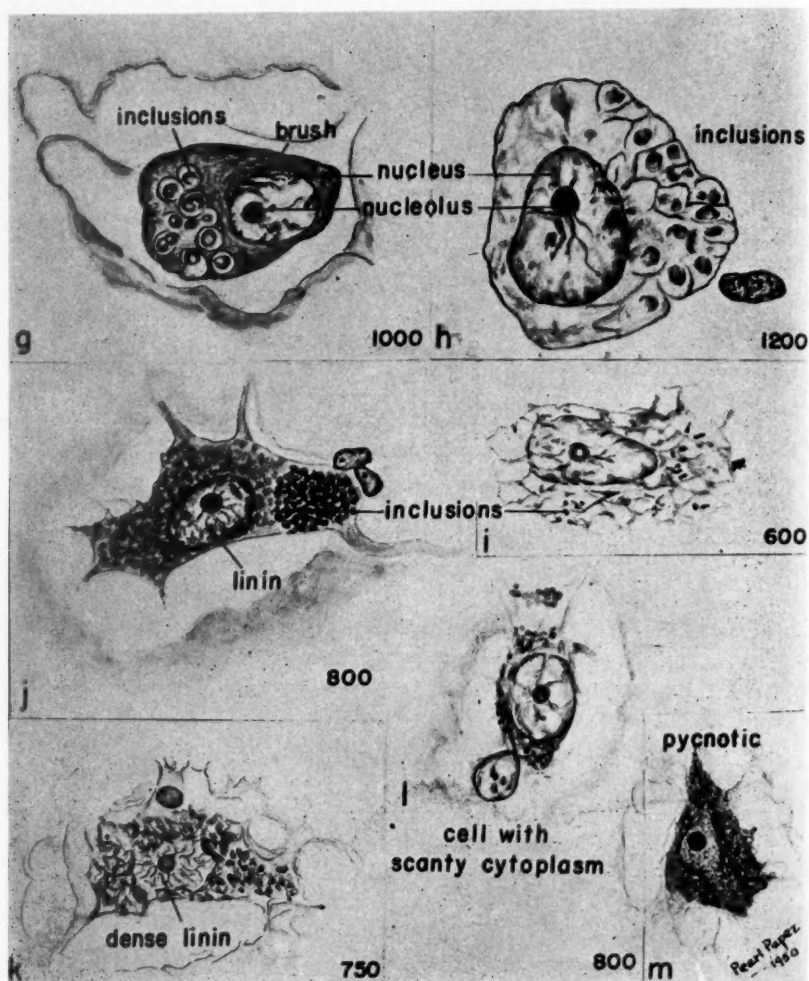


FIG. 5. Single nerve cells from senile, deteriorated types of psychoses; g, h, and i, cells from association nuclei of thalamus showing stages leading to breakdown; j, k, and l, nerve cells in manic types of psychoses showing small nuclei with increased linin network and destruction of cytoplasm; m, a pycnotic cell, X800.

acter of clinical symptoms. A disturbed function of the cells may be inferred as responsible for the discharging lesions causing auditory hallucinations.

The skin is an extensive covering of the body, made sensitive by the receptors for touch, warmth, cold and pain. The cutaneous nerves and spinothalamic paths transmit the different impulses from the skin to the ventral posterior nucleus of the thalamus (Fig. 1 vp) which relays them (sv) to the post-central cortex. Similar afferent impulses from the facial region are gathered by the trigeminal nerve and transmitted by trigeminal tracts to the arcuate nucleus of the thalamus (arc) which relays them to the lower part of the postcentral cortex.

Deep sensibilities of posture and movement come from receptors found in the muscles, tendons, fascias and ligaments. Nerves of deep sensibility conduct these impulses into the dorsal white columns of the cord which end in the nuclei gracilis and cuneatus. These nuclei relay them to the ventral posterior nucleus of the thalamus (Figs. 1 and 2 vp), from where they are sent on to the postcentral cortex. The awareness of the body, and posture muscles and their movements have a wide representation in the postcentral cortex. In fact, so elaborate are these cerebral patterns of the bodily framework in all its acts, that ideas of movement,<sup>5</sup> willing of movement and the body schema<sup>6</sup> are the outstanding expressions of cerebral activity of this region. In combination with cutaneous sensibilities, the functions of recognition and manipulation of objects are developed. The movements of locomotion, prehension and speech have their perceived patterns mainly in the parietal lobe. This is true for all bodily acts, skills and postures. Projection outward to all parts of the body is a prominent feature of the body schema as well as of the body image derived from the visual sphere.<sup>3</sup>

The cortical representation of the vestibular impulses may also be considered here. Correlation of abnormal bodily sensations in the patient with severe damage in the ventral posterior nucleus (vp) was suggested in a number of cases where there was more than usual damage in these cells (Fig. 4c). Most of these patients had minor symptoms of this nature.<sup>7</sup> Marked disturbances of the bodily schema were not recorded in our cases, but references to disordered bodily experiences were frequently recorded. More cases of this kind will have to be examined before any reliable conclusion can be reached.

Visceral sensibilities are brought into the central nervous system largely by the vagus and other enteric nerves. The larynx, lungs, heart, stomach and pelvic viscera have a varying degree of representation. Central paths from the vagal region and the gustatory nuclei pass upward, probably to the central and laminar nuclei of the thalamus which relays them to the insular and temporal cortex. The localization of visceral sensibilities in these cortical areas has recently received confirmation from well documented sources.<sup>8</sup> The visceral paths and thalamic relays are not yet well established. However, no doubt remains that such bodily needs as taste, thirst, hunger and visceral tensions express themselves through cortical representation. Normal visceral activity is in part monitored by impulses from the hypothalamus and serves to build up visceral experiences connected with emotional states.<sup>9</sup>

Very severe destruction of hypothalamic cells was found in most of the brains of markedly deteriorated patients who had lived an emotionally, non-reactive life in the hospital.

Emotional disturbance appeared to be related to changes in the nerve cells of the hippocampal region (Fig. 4d). In eleven patients who showed various symptoms of emotional disturbance,

the hippocampus was examined histologically. The findings were such as to indicate that disease of the hippocampus has some relation to intense hostility, assaultiveness, etc.<sup>10</sup>

Planned movement is the basis of volition.<sup>5</sup> Planned movement arises in the deep layers of the parietal lobe on the basis of perceived muscle sense within the body schema and body image. The pattern of this plan is projection on the lateral lobes of the cerebellum by the parietoponto-cerebellar path.<sup>11</sup> The cerebello-dento-rubro-thalamo-cortical path carries this pattern to the precentral motor cortex where it potentiates the impulses in the final common path to the skeletal muscles, namely the corticospino-muscular path.<sup>12</sup> The ventral lateral nucleus of the thalamus is the relay center for the impulses from the cerebellum to the cortex.<sup>13, 14</sup> Any disturbances of the voluntary pattern may have its source in the deep stratum of the parietal lobe, the cerebellum, the ventral lateral nucleus of the thalamus (vp), the precentral motor cortex or the cells of the motor nerves.

We have examined the nerve cells of the ventral lateral nucleus of the thalamus in ten cases (Fig. 4e). The results suggested that this nucleus may play an important part in voluntary movement. In most of the cases, disease in this nucleus could have been related to the disturbed behavior of the patient. In most cases we failed to examine the parietal and precentral motor areas and any attempt at a correlation is not possible.

The inner division of the pallidum also projects on the ventral anterior nucleus of the thalamus (Fig. 1va), which in turn sends its patterns of impulses to the precentral motor cortex. There are reasons for believing that these are inhibitor impulses concerned at least in part, with the fronto-ponto-cerebellar tract. This would have a function combined with voluntary movement.<sup>15</sup> Disturbance of suppressor or inhibitor functions is another common symptom in psychoses as exhibited by the phenomena of catatonia, especially when layers III and IV of the cortex are severely destroyed.<sup>14</sup>

The association nuclei of the thalamus are those cellular masses (pulvinar, lateral posterior, lateral anterior and medial dorsal) which receive cortico-thalamic fibers from the association areas of the cortex. Since these cellular masses do not receive any direct paths from the sense organs, they are generally regarded as related to the silent areas of the cortex. It is, however, true that the sensory areas of the cortex project fibers back to the association nuclei of the thalamus. One of the best known of these projections illustrated in most textbooks is that from the visual area in the occipital pole to the pulvinar. These fibers accompany the visual radiations to the lateral geniculate body where they turn dorsally to spread over the lateral or optic portion of the pulvinar (Figs. 1 and 2 pv.). In a like manner the area of bodily sensibilities in the postcentral cortex projects on the lateral posterior nucleus, a forward continuation of the pulvinar. There is evidence that the auditory area in the temporal lobe sends fibers to the pulvinar.

The pulvinar receives fibers and impulses from the cortex of the superior parietal lobule, inferior parietal lobule, superior temporal gyrus and the precuneus. In fact, the connections are in both directions, cortico-thalamic and thalamic-cortical. It will be observed that these gyri begin at one of the three sensory areas (visual, auditory or bodily sensibility), and pass across the cortex to join the other sensory areas. It is easy to see why a major interruption in these transcortical, intersensory highways may produce various types of receptive aphasia.<sup>16</sup> Many

examples of this occur in clinical literature. Large lesions in these gyri also lead to atrophy of the pulvinar.<sup>17</sup>

In fifteen cases of psychoses with mental deterioration, the greatest loss of nerve cells was found in the pulvinar (Fig. 5 gh). Perceiving, remembering, comprehending and symbolic functions were markedly affected. These obvious transcortical functions depended to a large extent on the association cortex of the parietal and temporal regions and its connection with the pulvinar. Cell demise was probably a slow process over a period of months or years, and damage of cortical cells was a contributing factor.

In senile psychoses of relatively late or sudden onset, marked by confusion, delusions, disturbed behavior, irritability, disorientation, loss of memory and symbolic functions, there was an acute breakdown or shattering of nerve cells in the pulvinar, lateral posterior and medial dorsal thalamic nuclei.

The parietal cortex which joins the postcentral cortex is known to subserve the functions of stereognosis or object recognition. In addition, it is the site of formation of body schema and planned movements. This cortex sends fibers and impulses to the lateral posterior nucleus of the thalamus (Fig. 1 lp). Disease of nerve cells in this nucleus was usually associated with disease of cells in the pulvinar. In some of the cases studied, somatic disturbances were indicated in the clinical histories. So generalized was the cellular disease and destruction in these association nuclei that a specific correlation could not be made in most cases.

The medial dorsal nucleus of the thalamus (Figs. 1 and 3 mc) sends the strong anterior thalamic radiations (ar) to the prefrontal cortex. In general, a very extensive disease or destruction of nerve cells was found here in all deteriorated cases of dementia praecox (Fig. 5 i). Also, the prefrontal cortex was severely affected in these cases. It seemed that dementia praecox had a predilection for these areas of the cortex and thalamus. However, it must be borne in mind that the disease is a generalized one affecting other thalamic nuclei and other areas of the cortex.

So far we have said nothing about transthalamic association.<sup>14</sup> Evidence bearing on this is rather scanty. It seems that the pulvinar, lateral posterior and lateral anterior nuclei connect by short fibers with the medial dorsal nucleus.<sup>17</sup> In this way the activities of the parietal cortex and precentral motor cortex may gain a representation in the prefrontal cortex. Or, they may serve as reservoirs upon which the prefrontal cortex may draw for its more planned functions, related to experience and behavior. This might be an important factor, especially in schizophrenia.

The thalamus and cortex of four cases of manic-depressive psychosis were studied. In three of these the thalamic nuclei showed a vast and comprehensive destruction of their nerve cells with surviving irregular, ragged and scanty cytoplasm filled with inclusion bodies (Figs. 5 j, k, l). Cell debris and degenerating inclusions were scattered through the intervening cell spaces. In the cortex the cells were greatly dwarfed.<sup>1</sup> They were reduced to bare nuclei with rims of cytoplasm and some inclusions. The cell nuclei were small and often filled with dense linin network (possibly a histone) and exhibited near pycnotic changes (m). In all four cases, the cortex showed all layers of cells with small exhausted, hyalinized nuclei and dwarfed cytoplasm often teaming with inclusion bodies in its ragged outer surface. The destruction of nerve cells



with small hyalinized nuclei and scanty tattered cytoplasm indicated that a prolonged, gradual destruction of nerve cells was characteristic of these cases of manic psychosis.

In five cases of psychosis with syphilitic meningo-encephalitis, the disease of nerve cells in the thalamic nuclei and cortex did not differ much from that in other psychoses. The presence of fenestrated cytoplasm, as if partial recovery had taken place, and often small exhausted cells approaching the pycnotic stage were noted. The inclusion bodies were sometimes small, suggesting a recurrent attack. One of the outstanding features was the thickened pia with great fenestration of the outer layers of the cortex and thickened walls of blood vessels. In four cases this fenestration was present over the motor area.

Axons in the thalamic radiations, internal capsule and basis pedunculi were studied by the Bielschowsky silver method in five cases. This stain revealed the axons with great clarity, especially in the bundles in the thalamic nuclei. In the paranoid psychoses, damage to the terminal neuropil was chiefly around the cell groups in the thalamus. The axons in the basis pedunculi, internal capsule and radiations were numerous and generally normal in thickness. Some distortion and pathological thickening of axons occurred in association with amyloid bodies in the fiber tracts. Where nerve cells were few, the axons in the radiations were markedly reduced. This was apparent in the thalamus of the senile cases with deterioration. Numerous gray spots without the usual bundles of axons were present. A heavy accumulation of amyloid bodies or gliosis usually marked an area of severe loss of axons. The number of axons in the thalamus was much in excess of the number of nerve cells. So, one got the impression of marked cell reduction associated with an abundance of axons many of which, no doubt, were of cortical origin, fibers of the cortico-thalamic projections. It was difficult to demonstrate neurofibrils in the affected nerve cells.

Disease of thalamic and cortical cells in psychoses was accompanied by changes in the oligoglia tubing within which the thalamic-cortical and cortico-thalamic axons passed by way of the internal capsule. These oligoglia tubes contained the myelin which surrounded the axons. A conspicuous abnormal feature in psychoses was the increase in the number of oligoglia nuclei, so that nests of three or four nuclei appeared where normally one nucleus would be encountered.<sup>18</sup> These nests of nuclei were usually enclosed in a clear fluid space to one side of which their cytoplasm was attached. Usually these nests bulged into the empty lumen of the oligoglia tube. In many cases these glia changes were striking. The foregoing oligoglia changes together with changes in the nerve cells were pathognomic of psychoses.

Necrosis of small areas of the thalamus, embolic and ischemic in nature, was seen in a few cases. It presented a picture of necrosis of nerve cells different in most respects from disruption and demise of nerve cells associated with inclusion bodies. Coagulation and fragmentation of cytoplasm, nucleus and inclusion bodies were present. Argentophile debris resulted from the shattered inclusion bodies. Microglia cells were present. An intense proliferation of glia fibers, with amyloid degeneration of nuclei of oligoglia cells occurred.

The ependymal lining of the medial and dorsal surface of the thalamus was often raised and blistered over the areas of gliosis. It was evident that fluid or lymph from the thalamus seeped through the glia fibers, stretched and tore the ependymal cells and entered the ventricles.

Senile plaques in various stages of formation were a feature associated with necrotic changes.

They were seen in the cortex but rarely in the thalamus. Three stages were encountered. First, the necrotic debris of nerve cells disappeared, leaving a space crossed by strands of local glia fibers. When near a blood vessel, this space in some cases was filled with a radiating exudate of thromboplastic material coming from the blood vessel. When this substance was absorbed, it left in its place the framework of a typical plaque as usually illustrated. Not all senile plaques gave evidence of having been occupied by the thromboplastic material.

The walls of the blood vessels usually showed patches of inclusion bodies embedded in them.<sup>19</sup> The inclusions were in the cytoplasm of the connective tissue cells and proliferation of the nuclei of these cells was a common feature. In a few cases there was also proliferation of the intima cells. It was evident that the inclusions produced thickenings and deformities in the walls of the small and medium sized vessels.

#### SUMMARY

The thalamic nuclei in twelve cases of dementia praecox, paranoid type, were examined histologically by special methods. All showed an old chronic disease of nerve cells filled with large groups of inclusion bodies sequestered in the cytoplasm. Usually there was a single group in each cell, and the individual inclusions, though closely crowded together, were very large in some cases. Actual loss of cells or breaking of their surfaces was moderate. In fact, most of the cells were intact and it seemed evident that the cells had tolerated the inclusions for a long time. Honey-combed cytoplasm and slightly vesicular nuclei in old cases with brush-work within the nuclear membrane were usually present. In the cortex, changes were more severe resulting in cell destruction, voiding of inclusions and loss of dendrites and axons. These changes affected the small cells of layers four and three. It seemed reasonable to infer that the hallucinations, delusions and paranoid symptoms were the result of abnormal discharges of thalamic and cortical cells.

In fifteen cases of psychoses with mental deterioration there was always a great loss of nerve cells, as high as 90 per cent of the cell population, in the association nuclei of the thalamus. The pulvinar and medial dorsal nuclei were often severely destroyed. The cell destruction was probably a slow process with minimal irritation in the thalamus. Damage of all layers of cells in the cortex was a contributing factor. In a number of the cases, necrosis of cells independent of the inclusion bodies, oligogliosis and senile plaques occurred. Argentophile debris and senile plaques were associated with necrosis, but they were not the usual causes of cell disease and disruption. The latter was a somewhat specific antecedent process related to the inclusion bodies and some hyperergic substance causing the formation of abnormal protein. Distorted growth of honey-combed cytoplasm, brush-work in nuclei, growth of glia fibers, amyloid changes in nuclei of oligoglia cells and proliferation of perivascular and microglia cells indicated abnormal growths of protein.

In cases with sensory disturbances, especially hallucinations and related delusions, there was an acute disruption of nerve cells in the sensory nuclei of the thalamus. This breaking down of nerve cells was seen in the lateral geniculate body (visual relay to cortex), in the medial geniculate body (auditory relay to cortex) and in the ventral posterior nucleus (relay for bodily sensibilities to the cortex). The ventral lateral nucleus (relay of cerebellar impulses to cortex) was usually affected.

In senile psychoses of relatively late and sudden onset, with confusion, irritability, disorientation, delusions, loss of memory and symbolic functions, there was an acute breakdown and shattering of nerve cells in the association nuclei of the thalamus. Usually this wholesale disruption of nerve cells filled with large inclusion bodies was most prominent in the pulvinar, lateral posterior and medial dorsal nuclei of the thalamus. Violent behavior seemed to be associated with an acute shattering of cells. Mental deterioration was related to the more complete loss of cells.

Four cases of manic-depressive psychosis showed disease of thalamic cells similar to those of other clinical types. Pycnotic changes were more common. The nerve cells had small, hyalinized nuclei with dwarfed rims of cytoplasm around them. The cells of the cortex were particularly small with the pycnotic nuclei.

Five cases of psychosis with syphilitic meningo-encephalitis differed from the other psychoses chiefly in the thickened meninges and blood vessels and fenestration of the outer layers one and two of the cortex.

Axons were studied by the silver technique in the thalamic region in five cases. This included the thalamic radiations, internal capsule, basis pedunculi and adjacent structures. Axonal damage was not a conspicuous feature but where it occurred, it was unmistakable. Dropping out of axons from the bundles of radiations, and deformity of axons with enlargements and twistings were abnormal features. Damage to axons occurred in the neighborhood of the diseased nerve cells. The number of axons in the thalamus was much in excess of nerve fibers, due to presence of fibers coming from the cortex. Terminal neuropil among the thalamic cells was severely affected.

Disruption of cortical cells and changes in radial bundles were contributing factors in most of the cases. From a limited number of sample sections, it was not possible to gain a reliable idea of the distribution of cortical disease. Our samples usually included the occipital, temporal, parietal, frontal and hippocampal cortices, but not all parts in all cases. However, it was clear that the cortex was severely involved in cases with simple mental deterioration and in Alzheimer's disease. Gliosis, amyloid bodies, necroses and senile plaques were occasionally seen in these cases. In some instances, it seemed that the onset of cortical destruction with small inclusion bodies was a new episode with exacerbation of an old brain disease.

The thirty-six cases examined histologically showed that disease of thalamic nerve cells was a constant feature of various clinical types of psychoses. In all cases, cortical cells were also involved. Correlation of clinical symptoms with disease of the sensory and association nuclei was strongly suggested by this study. However, it must be stated that the disease was generalized, affecting both thalamus and cortex in various degrees. There was no specific pattern for any type, but only a predominance of cell affection in different areas of the thalamus and cortex, and difference in degree of cell destruction. It seemed that nerve cells were more involved than axons, and that the active symptoms exhibited by the patients were an expression of altered nerve cell function. This would favor the current views which hold that the functional manifestations of the psychoses are basically disorders reflecting fundamentally abnormal physiology and morphologic changes in the thalamo-cerebral level of the central nervous system. The chemical disorder and its hyperergic effects on nuclear (cell) metabolism, glia proliferation, changes in axons and walls

of the blood vessels must be taken into consideration. The moderate changes in the fiber tracts, changes such as demyelination, nests of oligoglia nuclei, and amyloid bodies appeared to result from some abnormal protein donated by the nerve cell disease.

## RESUMEN

El autor examinó histológicamente, por métodos especiales, el núcleo talámico en 12 casos de demencia precoz de tipo paranoide. Todos los casos presentaron signos de una vieja afección crónica de las células nerviosas con grandes grupos de cuerpos de inclusión secuestrados en el citoplasma. En la corteza cerebral los cambios fueron más agudos, y se observaron destrucciones celulares, con pérdida de las dendritas y axones. El autor deduce que las alucinaciones, ilusiones y síntomas paranoides, resultaron de descargas anormales de las células talámicas y corticales.

En 15 casos de psicosis con alteraciones mentales, existió siempre una destrucción del 90 por ciento de las células nerviosas y los núcleos asociados del tálamo. En los casos con alteraciones sensoriales, especialmente alucinaciones, hubo una disrupción aguda de las células nerviosas en el núcleo sensorial del tálamo. En las psicosis seniles de comienzo retardado y súbito, hubo una ruptura aguda de las células nerviosas en el núcleo de asociación del tálamo.

En 4 casos de psicosis maniaco-depresivas se observó una afección de las células talámicas, similar a la de los otros tipos clínicos. Cinco casos de psicosis con meningoencefalitis sifilítica presentaron engrosamiento meníngeo de los vasos sanguíneos y fenestración de las capas externas de la corteza cerebral.

Los 36 casos examinados histológicamente revelaron que las alteraciones de las células nerviosas talámicas constituían una característica constante en los diversos tipos clínicos de psicosis. Este estudio sugirió la existencia de una relación entre los síntomas clínicos y las enfermedades de los núcleos sensoriales y de asociación, que afectaba el tálamo y la corteza cerebral en grados diversos.

En ninguno de los casos existía un cuadro específico, sino solamente un predominio de las lesiones celulares en diferentes áreas del tálamo y del córtex cerebral y una diferencia en el grado de la destrucción celular. Las células nerviosas aparentemente estaban más afectadas que los axones, y los síntomas activos que presentaban los pacientes eran una manifestación de la alteración de las funciones de las células nerviosas. Ello habla en pro de la opinión actual de que las psicosis son básicamente trastornos funcionales originados por una anomalía fisiológica del nivel talámico-cerebral del sistema nervioso central.

## RESUME

On a procédé à un examen histologique par des méthodes spéciales des nucléus thalamiques pour 12 cas de démence précoce du type paranoïde. Tous ces cas ont révélé une affection chronique ancienne de cellules nerveuses envahies par des groupes importants de corps d'inclusion enchâssés dans le cytoplasme. En général, il y avait un seul groupe dans chaque cellule, et les inclusions séparées, bien que très rapprochées les unes des autres, étaient très grandes dans certains cas. Dans la substance corticale, les changements observés ont été plus marqués, se traduisant par la destruction de cellules, et la perte de dendrites et d'axones. Il a semblé logique

de conclure que les hallucinations, les illusions et les symptômes paranoïdes étaient la conséquence de pertes anormales des cellules thalamiques et corticales.

Dans 15 cas de psychoses accompagnées d'altération des facultés intellectuelles, on a régulièrement constaté une perte élevée de cellules nerveuses, allant parfois jusqu'à 90% du nombre de cellules, dans les nucléus d'association du thalamus.

Dans les cas accompagnés de dérangements sensoriels, en particulier des hallucinations et illusions dérivées, on a observé une dislocation marquée des cellules nerveuses dans les nucléus sensoriels du thalamus.

Dans les psychoses séniles de manifestation brusque et relativement tardive, accompagnées de confusion, d'irritabilité, de désorientation, d'illusions, de perte de la mémoire et des fonctions symboliques, on a observé un ébranlement marqué des cellules nerveuses dans les nucléus d'association du thalamus.

Quatre cas de psychose maniaque-dépressive ont révélé une lésion des cellules thalamiques analogue à celles des autres cas cliniques. Les modifications pycnotiques étaient plus fréquemment observées. Les cellules nerveuses présentaient de petits nucléus hyalinisés avec des bords rabougris de cytoplasme tout autour.

Cinq cas de psychose avec méningo-encéphalite syphilitique se sont différenciés principalement des autres psychoses par l'épaississement des méninges et des vaisseaux sanguins et l'état fenêtré des couches extérieures de la substance corticale.

Les 36 cas soumis à un examen histologique ont révélé que l'affection des cellules nerveuses thalamiques est une caractéristique constante des divers types cliniques de psychoses. Cette étude a révélé une corrélation étroite des symptômes cliniques avec l'affection des nucléus sensoriels et d'association. Toutefois, il y a lieu de signaler que l'affection était généralisée et qu'elle affectait à des degrés divers tant le thalamus que la substance corticale. On n'a pas observé de type bien déterminé, mais on a seulement constaté la prédominance de l'affection des cellules dans diverses régions du thalamus et de la substance corticale, et un degré varié de la destruction des cellules. Tout ceci semble confirmer l'opinion courante que les psychoses sont essentiellement des dérangements fonctionnels basés sur une physiologie anormale de l'échelon thalamo-cérébral du système nerveux central.

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